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A

LEADER : 8187 DIV

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: SABIHA QAZI Examiner #: 74141 Date: 10/7/05
Art Unit: 1616 Phone Number: 2-0622 Serial Number: 10/500532
Location (Bldg/Room#): 4A45 (Mailbox #): 4C70 Results Format Preferred (circle): PAPER DISK
****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Process for the preparation of 1-[3-dimethyl-aminopropyl]-

Inventors (please provide full names): SIRINIVASU et al

Earliest Priority Date: 1/7/02 371 of PCT/IN03/00006

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Cls 546 1-3, 5-22, 41, 42, 44, 45 & 47.

Please search for the process of making the compd of formula I as in cl 1, 2, 3 41.

Common name of the compd

CITALOPRAM. (see cls 45, 47)

Please see attached sheets

Thank you

****

Qazi, S.
10/500532

FILE 'REGISTRY' ENTERED AT 12:47:25 ON 18 OCT 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 OCT 2005 HIGHEST RN 865410-76-0
DICTIONARY FILE UPDATES: 17 OCT 2005 HIGHEST RN 865410-76-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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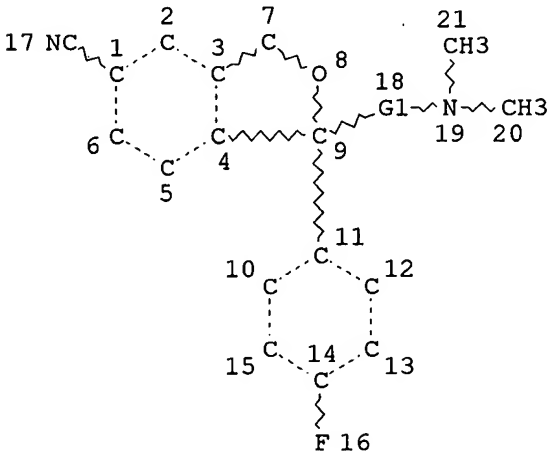
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1 STR



Form I.

REP G1=(3-3) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM

Searcher : Shears 571-272-2528

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
L2 55 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 222 ITERATIONS 55 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 12:47:25 ON 18 OCT 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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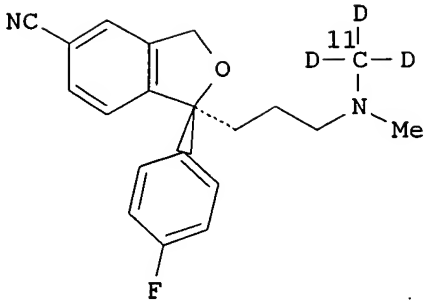
FILE COVERS 1907 - 18 Oct 2005 VOL 143 ISS 17
FILE LAST UPDATED: 17 Oct 2005 (20051017/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

L3 100 S L2/P
L4 13 S L3 NOT (PY=>2002 OR PD=>20020107) ← Eliminate citations dated on or after 01-07-02

L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:174806 CAPLUS
DOCUMENT NUMBER: 137:369908
TITLE: Gas phase production of 11CD3I and synthesis of S-[N-D3-methyl-11C]citalopram
AUTHOR(S): Madsen, Jacob; Andersen, Kim; Knudsen, Gitte M.; Martiny, Lars
CORPORATE SOURCE: PET & Cyclotron Unit, Copenhagen University Hospital, Copenhagen, DK-2100, Den.
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001), Meeting Date 2000, 347-350. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:369908
GI



I

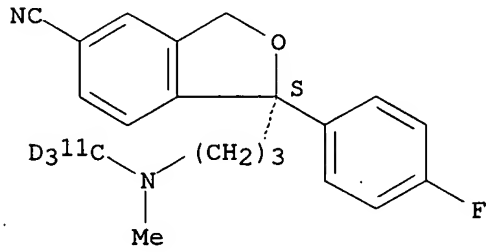
AB The preparation of 11CH3I in a gas phase reaction was expanded to include the formation of 11CD3I. Bombarding a mixture of N2 and D2 with 16 MeV protons in a gas target and trapped on a porapak N column at -190° yielded 11CD4. After warmup, the 11CD4 and I2 vapors were in several cycles passed through a quartz tube at 720 °. At the end of each reaction cycle 11CD3I was trapped on the Porapak N column at room temperature At the point when reacted 11CD4 was recirculated through the quartz tube, the 11CD3I was liberated by purging the Porapak trap at 190 ° with helium. S-N-Desmethyl-citalopram monofumarate was methylated in ethanol and 1,2,2,6,6-pentamethyl-piperidine (PMP) at reflux temperature producing S-[N-d3-methyl11C]citalopram I. After purification the radiochem. purity was > 99% and the radiochem. yield in the labeling step was 34%. The specific activity of the final product obtained was 0.65 Ci/μmol EOS with a 45 min total synthesis time. A higher specific activity (2.5-3.5 Ci/μmol EOS) of S-[N-methyl-11C]-citalopram was achieved when 11 CH3I was yielded with N2/H2 (95%/5%) as the target gas.

IT **475107-77-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isotopically labeled S-[N-D3-methyl-11C]citalopram via methylation of corresponding N-methylamine with 11CD3I)

RN 475107-77-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-d3-amino)propyl]-, (1S)- (9CI) (CA INDEX NAME)

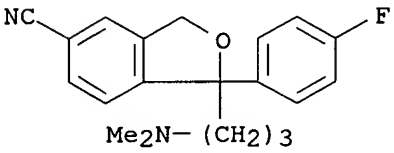
Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searcher : Shears 571-272-2528

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:740744 CAPLUS
DOCUMENT NUMBER: 136:95936
TITLE: A new alternative synthesis of 5-cyanophthalide, a versatile intermediate in the preparation of the antidepressant drug citalopram
AUTHOR(S): Micheli, F.; Crippa, L.; Donati, D.; Di Fabio, R.; Leslie, C.
CORPORATE SOURCE: GlaxoSmithKline Group, Medicines Research Centre, GlaxoWellcome SpA, Verona, 37135, Italy
SOURCE: Farmaco (2001), 56(9), 715-718
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An alternative versatile synthesis of 5-cyanophthalide, a key synthetic intermediate in the preparation of the antidepressant drug Citalopram, is presented. The synthesis reported here allows the preparation of this important intermediate in three steps, avoiding the manipulation of environmentally detrimental cyanides.
IT **59729-33-8P**, Citalopram
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(new alternative synthesis of 5-cyanophthalide, a versatile intermediate in preparation of antidepressant drug citalopram)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

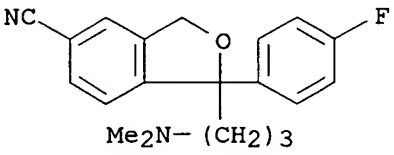
L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:558778 CAPLUS
DOCUMENT NUMBER: 135:192383
TITLE: Reduction of extraction times in liquid-phase microextraction
AUTHOR(S): Gronhaug Halvorsen, T.; Pedersen-Bjergaard, S.; Rasmussen, K. E.
CORPORATE SOURCE: School of Pharmacy, University of Oslo, Oslo, 0316, Norway
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 760(2), 219-226
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, the authors introduced a simple and inexpensive disposable device for liquid-phase microextn. (LPME) based on porous polypropylene

hollow fibers. In the present paper, extraction times were significantly reduced by an increase in the surface of the hollow fibers. The model compds. methamphetamine and citalopram, were extracted from 2.5 mL of urine, plasma, and whole blood after dilution with water and alkalization with 125 μL of 2M NaOH though a porous polypropylene hollow fiber impregnated with hexyl ether and into an aqueous acceptor phase consisting of 0.1M HCl. Two com. available hollow fibers, which differed in surface area, wall thickness and internal diameter, were compared. An increase in the contact area of the hollow fiber with the sample solution by a factor of approx. two resulted in reduction in equilibrium times by approx. the same factor. Thus, the model compds. were extracted to equilibrium within 15 min from both urine and plasma, and within 30 min from whole blood. For the first time LPME was utilized to extract drugs from whole blood, and the exts. were comparable with plasma both with regard to sample clean-up and extraction recoveries. Extraction recoveries for methamphetamine and citalopram varied from 60 to 100% using the two fibers and the different matrixes.

IT **59729-33-8P**, Citalopram
RL: PUR (Purification or recovery); PREP (Preparation)
(reduction of extraction times in liquid-phase microextn.)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:386023 CAPLUS

DOCUMENT NUMBER: 134:353251

TITLE: Method for the preparation of citalopram by nickel-catalyzed cyanation of halo precursors

INVENTOR(S): Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S): H Lundbeck A/S, Den.

SOURCE: Brit. UK Pat. Appl., 16 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

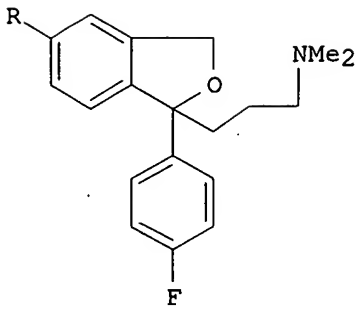
LANGUAGE: English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2354240 A1		20010321	GB 2001-1508	19991119
PRIORITY APPLN. INFO.:			DK 1999-921	19990625
			WO 1999-DK643	19991119

OTHER SOURCE(S): MARPAT 134:353251

GI



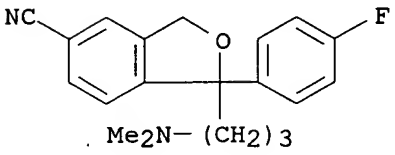
I

AB A method for the preparation of citalopram is presented, comprising the reaction of isobenzofuranpropanamine I, wherein R is Cl or Br, with a cyanide source in the presence of a nickel catalyst and isolation of the corresponding 5-cyano compound, i.e. citalopram.

IT **59729-33-8P**, Citalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(method for the preparation of citalopram by nickel-catalyzed cyanation of halo precursors)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:289970 CAPLUS

DOCUMENT NUMBER: 134:311097

TITLE: Preparation of phthalans, their intermediates, and citalopram

INVENTOR(S): Ikemoto, Tetsuya; Kobori, Kazuhiro; Iki, Masaki

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

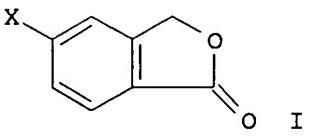
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001114773	A2	20010424	JP 1999-292076	19991014
PRIORITY APPLN. INFO.:			JP 1999-292076	19991014

OTHER SOURCE(S): CASREACT 134:311097; MARPAT 134:311097

GI

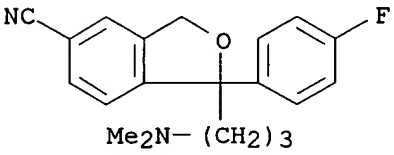


AB Citalopram is prepared from phthalides I (X = protected formyl group) via 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbaldehyde (II). 5-(1,3-Dioxolan-2-yl)phthalide was reacted with reagent containing 1-bromo-4-fluorobenzene and Mg in THF at room temperature for 2 h, reacted with reagent containing 3-(dimethylamino)propyl chloride and Mg at room temperature for 18 h, and treated with H3PO4 at 80° for 2 h to give 65% II, which was reacted with hydroxylamine hydrochloride in the presence of Et3N in acetonitrile at room temperature for 15 h to give 89% citalopram.

IT **59729-33-8P**, Citalopram
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation citalopram from phthalides via isobenzofurancarbaldehyde)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:270419 CAPLUS

DOCUMENT NUMBER: 134:280701

TITLE: Preparation of 5-cyanophthalide and its intermediates, 5-halogenomethylphthalide and 5-formylphthalide using no toxic substances

INVENTOR(S): Ikemoto, Tetsuya; Kobori, Kazuhiro; Iki, Seimi

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001106681	A2	20010417	JP 1999-287313	19991007
PRIORITY APPLN. INFO.:			JP 1999-287313	19991007

OTHER SOURCE(S): CASREACT 134:280701; MARPAT 134:280701

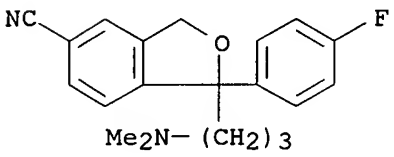
AB 5-Cyanophthalide, useful as an intermediate for citalopram (antidepressant), is prepared by dihalogenation of 2,4-dimethylbenzoic acid or its lower alkyl esters, cyclization, formylation of the

resulting 5-chloro- or 5-bromomethylphthalide, and cyanation. Thus, formylation of 5-bromomethylphthalide with hexamethylenetetramine and H2O in 80% AcOH under reflux for 2 h gave 81% 5-formylphthalide, which was treated with NH2OH.HCl in the presence of Et3N at 65° for 1 h in MePh and further treated with Ac2O at 120-125° for 3 h to afford 69% 5-cyanophthalide.

IT **59729-33-8P**, Citalopram
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of 5-cyanophthalide as intermediate for citalopram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:181925 CAPLUS

DOCUMENT NUMBER: 135:70537

TITLE: On-line extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma. Results compared with solid-phase extraction methodology

AUTHOR(S): Ohman, D.; Carlsson, B.; Norlander, B.

CORPORATE SOURCE: Faculty of Health Sciences, Department of Medicine and Care, Clinical Pharmacology, Linkoping University, Linkoping, S-581 85, Swed.

SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 753(2), 365-373
CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

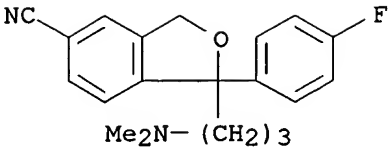
LANGUAGE: English

AB Sample preparation is usually the most critical and time consuming step when using HPLC for drug anal. in biol. matrixes. Sample exts. have to be clean considering both chromatog. interferences and column maintenance. To meet some of these criteria a fully automated online extraction (OLE) anal. method was developed for the antidepressant drug citalopram and its two demethylated metabolites, using an RP-C4-ADS extraction column. A comparison between the new OLE method and an off-line solid-phase extraction method showed that the two methodologies were equal in anal. precision but that the OLE method was faster and therefore superior in sample capacity per day.

IT **59729-33-8P**, Citalopram
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(online extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma and comparison with solid-phase extraction methodol.)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



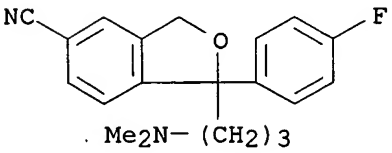
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:665746 CAPLUS
DOCUMENT NUMBER: 132:6266
TITLE: Racemic switches. Historical perspectives and current status
AUTHOR(S): Cannarsa, Michael J.
CORPORATE SOURCE: PPG-Sipsy Chemical Co., West Chester, PA, 19382, USA
SOURCE: Chimica Oggi (1999), 17(9), 28-32
CODEN: CHOGDS; ISSN: 0392-839X
PUBLISHER: TeknoScienze
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 6 refs., describing historical development of asym. synthesis technol. and recent developments in racemic switches of perprazole, fluoxetine, D-methylphenidate, levalbuterol, levobupivacaine, citalopram, cetirizine, norcisapride-(+), zopiclone, and formoterol-(R,R). The single enantiomers (S)-ibuprofen, dexketoprofen, dexfenfluramine, and verapamil continue to struggle for a place in the market.

IT **59729-33-8P**, Citalopram
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(racemic switches in drug production, historical perspectives and current status)

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

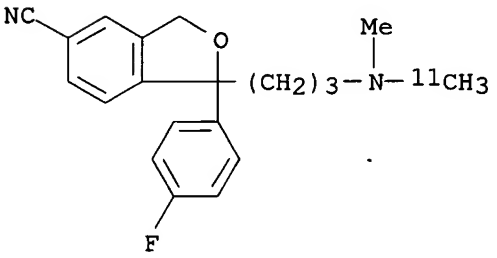
L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:467618 CAPLUS
DOCUMENT NUMBER: 115:67618
TITLE: Citalopram: labeling with carbon-11 and evaluation in rat as a potential radioligand for in vivo PET studies of 5-HT re-uptake sites

AUTHOR(S): Hume, S. P.; Pascali, C.; Pike, V. W.; Turton, D. R.; Ahier, R. G.; Myers, R.; Bateman, D. M.; Cremer, J. E.; Manjil, L. G.; Dolan, R.
CORPORATE SOURCE: MRC Cyclotron Unit, Hammersmith Hosp., London, W12 0HS, UK
SOURCE: Nuclear Medicine and Biology (1991), 18(3), 339-51
CODEN: NMBIEO; ISSN: 0883-2897
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vivo autoradiog. of [N-methyl-3H]citalopram in rat brain shows a differential regional localization which correlates with the localization of 5-HT re-uptake binding sites defined in vitro. A comparison of the biodistribution of [N-methyl-3H]citalopram over 2 h after i.v. injection in control rats rats predosed with either citalopram or paroxetine, and rats chemical lesioned with p-chloroamphetamine provides an estimate of specific binding relative to total binding in vivo. The ratio of binding in certain regions (e.g., cingulate) to binding in a reference tissue (e.g., cerebellum) at 30-120 min postinjection is .apprx.1.4. In view of these results, a method was developed for labeling citalopram with 11C (t1/2 = 20.3 min, β+ = 99.8%) to provide a potential radioligand for studies using positron emission tomog. Thus, reaction of no carrier added [11C]iodomethane, prepared from cyclotron-produced 11CO2, with norcitalopram in EtOH containing 2,2,6,6-tetramethyl-piperidine for 5 min at 95°, gives crude [N-methyl-11C]citalopram in 60% radiochem. yield, decay-corrected HPLC on silica gel provides radiochem. and CP [N-methyl-11C]citalopram, as assessed by TLC, HPLC, and MS. This product (isolated radiochem. yield, 49%) is easily formulated for i.v. injection. Up to 2 GBq of formulated product with a specific activity of .apprx.15 GBq/μmol have been prepared within 40 min from the end of radionuclide production The described radiosynthesis has also been applied to give the single biol. active (+)-enantiomer of [N-methyl-11C]citalopram rather than the racemate. This product gives enhanced specific signal in the rat following i.v. injection, the ratio of uptake in regions of interest relative to cerebellum approaching 2 at 90 min.

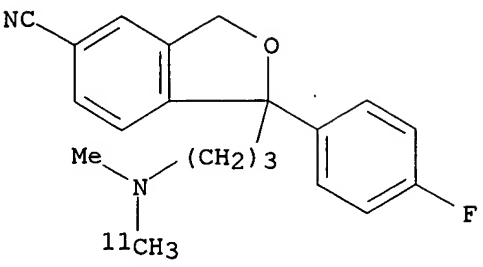
IT **129356-76-9P 134915-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biodistribution of and positron emission tomog. with, of serotonin reuptake sites in brain)

RN 129356-76-9 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-amino)propyl]- (9CI) (CA INDEX NAME)

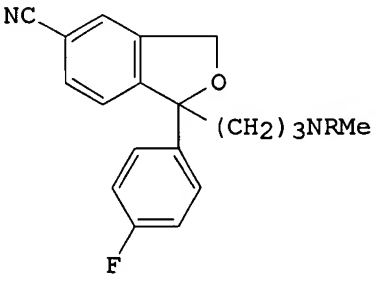


RN 134915-04-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-amino)propyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:631122 CAPLUS
DOCUMENT NUMBER: 113:231122
TITLE: Synthesis of carbon-11 labeled citalopram, a selective serotonin uptake inhibitor
AUTHOR(S): Ram, Siya
CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA
SOURCE: Applied Radiation and Isotopes (1990), 41(7), 645-8
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

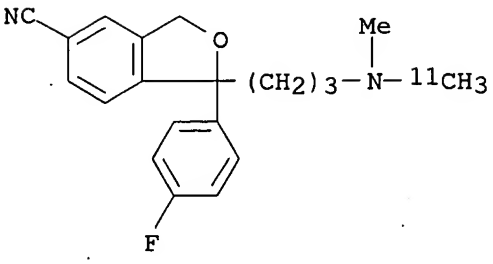


I, R=Me
II, R=H
III, R=11CH3

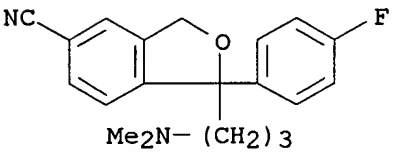
AB A procedure for labeling the novel serotonin uptake inhibitor, citalopram (I), with the positron emitting radionuclide 11C (t1/2 = 20.4 min) was developed, to permit the pharmacokinetics of this compound to be studied in man. The procedure involves the reaction of 11CH3I with desmethylcitalopram (II) in acetone in the presence of NaOH base at 65° for 8-10 min; this was followed by purification by a column which contained, in series silica gel and basic alumina, and produces no carrier added [11C]citalopram (III) in radiochem. yield (18-66% at EOB) and radiochem. purity (>95%). The specific activity of III was 2.52 + 103-16.06 + 103 GBq/mmol (68-434 Ci/mmol) at the end of synthesis.

IT **129356-76-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129356-76-9 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-

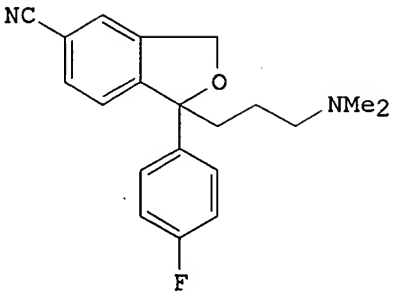
(methylmethyl-11C-amino)propyl]- (9CI) (CA INDEX NAME)



IT **59729-33-8P**, Citalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of carbon-11 labeled and unlabeled)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:526655 CAPLUS
DOCUMENT NUMBER: 113:126655
TITLE: Synthesis of a selective serotonin uptake inhibitor: carbon-11 labeled [11C]citalopram
AUTHOR(S): Dannals, Robert F.; Ravert, Hayden T.; Wilson, Alan A.; Wagner, Henry N., Jr.
CORPORATE SOURCE: Div. Nucl. Med. Radiat. Health Sci., Johns Hopkins Med. Inst., Baltimore, MD, 21205-2179, USA
SOURCE: Applied Radiation and Isotopes (1990), 41(6), 541-3
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



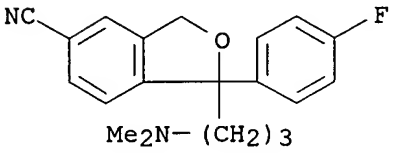
I

AB Citalopram (I), a selective serotonin uptake inhibitor, was labeled with 11C for noninvasive in the human brain using positron emission tomog. The synthesis was completed in .apprx.17 min using [11C]methyl iodide as the precursor. The synthesis, purification, characterization, and determination of specific activity are described.

IT **59729-33-8P**, Citalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as serotonin uptake inhibitor)

RN 59729-33-8 CAPLUS

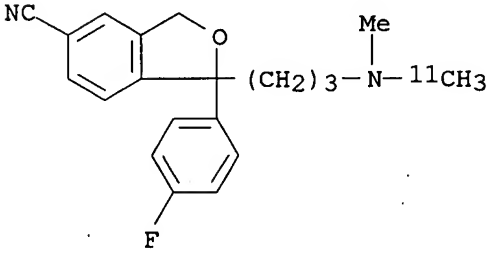
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



IT **129356-76-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as serotonin uptake inhibitor, for PET)

RN 129356-76-9 CAPLUS

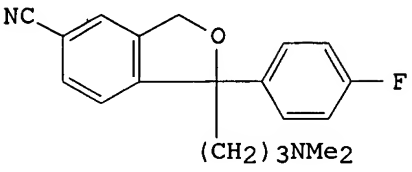
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-amino)propyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:561413 CAPLUS
DOCUMENT NUMBER: 87:161413
TITLE: Quantitative structure-activity relationships in a series of selective 5-HT uptake inhibitors

Searcher : Shears 571-272-2528

AUTHOR(S): Bigler, Allan J.; Boegesoe, Klaus P.; Toft, Anders; Hansen, Villy
CORPORATE SOURCE: Dep. Synth. Chem., H. Lundbeck and Co. A/S, Copenhagen-Valby, Den.
SOURCE: European Journal of Medicinal Chemistry (1977), 12(3), 289-95
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 87:161413
GI

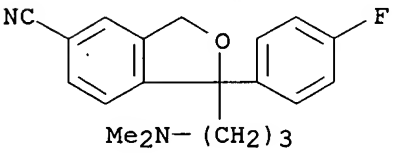


HBr I

AB Fifty-five 1-[3-(methylamino)propyl]- and 1-[3-(dimethylamino)propyl]-1-phenylphthalan derivs. were prepared and tested in vitro for inhibition of 5-hydroxytryptamine [50-67-9] uptake in blood platelets and in vivo for potentiation of 5-HTP syndrome in mice. Quant. structure-activity relations were established, using the methods of Free-Wilson and Hansch. Of several potent compds., Citalopram (I) [59729-33-8] was the most active.

IT **59729-33-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydroxytryptamine inhibition by)

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:535040 CAPLUS
DOCUMENT NUMBER: 87:135040
TITLE: Phthalan derivatives
INVENTOR(S): Boegesoe, Klaus Peter; Toft, Anders Stausboell
PATENT ASSIGNEE(S): Kefalas A/S, Den.
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

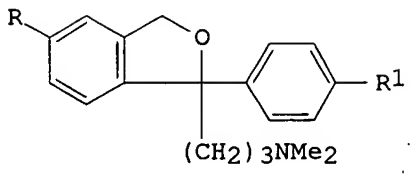
DE 2657013	A1	19770728	DE 1976-2657013	19761216
DE 2657013	C2	19851114		
SE 7614201	A	19770715	SE 1976-14201	19761217
SE 429551	B	19830912		
SE 429551	C	19831222		
AT 7609472	A	19800415	AT 1976-9472	19761221
AT 359488	B	19801110		
AU 7721073	A1	19780713	AU 1977-21073	19770105
AU 509445	B2	19800515		
US 4136193	A	19790123	US 1977-757619	19770107
FI 7700073	A	19770715	FI 1977-73	19770111
FI 63754	B	19830429		
FI 63754	C	19830810		
NL 7700244	A	19770718	NL 1977-244	19770112
NL 192451	B	19970401		
NL 192451	C	19970804		
NO 7700109	A	19770715	NO 1977-109	19770113
NO 147243	B	19821122		
NO 147243	C	19830302		
JP 52105162	A2	19770903	JP 1977-1997	19770113
JP 61035986	B4	19860815		
CA 1094087	A1	19810120	CA 1977-269610	19770113
CH 626886	A	19811215	CH 1977-423	19770113
BE 850401	A1	19770714	BE 1977-174098	19770114
DK 7700131	A	19770715	DK 1977-131	19770114
DK 143275	B	19810803		
DK 143275	C	19820118		
FR 2338271	A1	19770812	FR 1977-1079	19770114
FR 2338271	B1	19821105		
AT 7905719	A	19800515	AT 1979-5719	19790827
AT 360001	B	19801210		
AT 7905720	A	19800515	AT 1979-5720	19790827
AT 360002	B	19801210		
CH 632258	A	19820930	CH 1981-3574	19810601
CH 632259	A	19820930	CH 1981-3575	19810601

PRIORITY APPLN. INFO.: GB 1976-1486 A 19760114

AT 1976-9472 A 19761221

CH 1977-423 A 19770113

GI



I

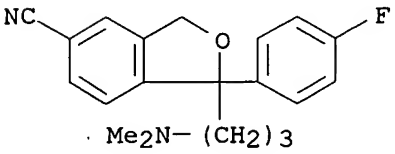
AB Phthalans I (R = Cl, Br, CF3, F, CN, COEt; R1 = Cl, F, Br, CN) were prepared Thus, 5-bromophthalide was treated with 4-ClC6H4MgBr, 4,2-Br(HOCH2)C6H3COC6H4Cl-4 treated with Me2N(CH2)3MgCl, and 4,2-Br(HOCH2)C6H3C(OH)(C6H4Cl-4)(CH2)3NMe2 cyclized with H3PO4 to give I (R = Br, R1 = Cl), which had ED50 in the tryptophan potentiation

test of 4.6 mg/kg i.p.

IT **59729-33-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antidepressant activity of)

RN 59729-33-8 CAPLUS

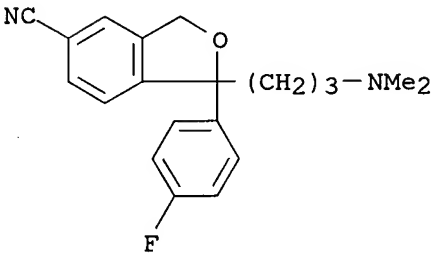
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



IT **59729-32-7P 64169-59-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)



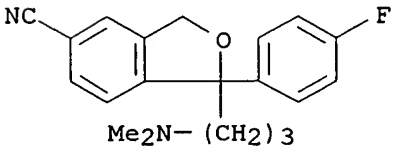
● HBr

RN 64169-59-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

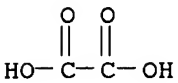
CM 1

CRN 59729-33-8
CMF C20 H21 F N2 O



CM 2

CRN 144-62-7
CMF C2 H2 O4



E1 THROUGH E6 ASSIGNED

FILE 'REGISTRY' ENTERED AT 12:51:14 ON 18 OCT 2005
L5 6 SEA FILE=REGISTRY ABB=ON PLU=ON (59729-33-8/BI OR 129356-76-9/BI OR 134915-04-1/BI OR 475107-77-8/BI OR 59729-32-7/BI OR 64169-59-1/BI)

FILE 'CAOLD' ENTERED AT 12:51:43 ON 18 OCT 2005
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L6 0 L5

FILE 'USPATFULL' ENTERED AT 12:51:50 ON 18 OCT 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US6957446
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229280
CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<

>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

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>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

L7 73 S L5/P
L8 10 S L7 NOT (PY=>2002 OR PD=>20020107)

L8 ANSWER 1 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2001:224233 USPATFULL
TITLE: Citalopram hydrobromide crystal and method for crystallization thereof
INVENTOR(S): Ikemoto, Tetsuya, Osaka-shi, Japan
Arai, Nobuhiro, Osaka-shi, Japan
Igi, Masami, Osaka-shi, Japan

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001049450	A1	20011206	
APPLICATION INFO.:	US 2001-824447	A1	20010402	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-133995	20000502

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LEYDIG VOIT & MAYER, LTD, TWO PRUDENTIAL PLAZA, SUITE 4900, 180 NORTH STETSON AVENUE, CHICAGO, IL, 60601-6780
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 789
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB According to the present invention, citalopram hydrobromide dissolved in a solvent containing at least one member selected from the group consisting of alcohol having 1-3 carbon atoms, water and acetone is crystallized or recrystallized while controlling the cooling rate, thereby to 1) provide an industrial method for crystallizing citalopram hydrobromide, which enables easy control of the crystal characteristics, such as particle size, particle size distribution and aspect ratio and the like of the crystal, and 2) provide citalopram hydrobromide crystal having crystal characteristics useful as a pharmaceutical bulk.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Searcher : Shears 571-272-2528

L8 ANSWER 2 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2001:191288 USPATFULL
TITLE: Production method of 5-phthalancarbonitrile compound, intermediate therefor and production method of the intermediate
INVENTOR(S): Ikemoto, Tetsuya, Osaka, Japan
Igi, Masami, Osaka, Japan
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6310222	B1	20011030
APPLICATION INFO.:	US 2000-648048		20000825 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-311703	19991101

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Solola, T. A.
LEGAL REPRESENTATIVE: Leydig, Voit & Mayer, Ltd.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 970
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a production method of a 5-phthalancarbonitrile compound, which comprises the use of a novel compound of the formula [I] ##STR1##

wherein X is chlorine atom, bromine atom or iodine atom, as a key intermediate; intermediate; and the process of preparing intermediates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 3 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2001:182624 USPATFULL
TITLE: Crystalline base of citalopram
INVENTOR(S): Petersen, Hans, Vanlose, Denmark
Bogeso, Klaus Peter, Horsholm, Denmark
Holm, Per, Vanlose, Denmark

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001031784	A1	20011018
APPLICATION INFO.:	US 2000-730490	A1	20001205 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2000-402	20000313

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DARBY & DARBY P.C., 805 Third Avenue, New York, NY, 10022
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 328
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The crystalline base of the compound citalopram, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile, having the formula ##STR1##

and its use in a process for the manufacture of a citalopram salt is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 4 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2001:158505 USPATFULL
TITLE:	Method for the preparation of citalopram
INVENTOR(S):	Petersen, Hans, Vanl.o slashed.se, Denmark B.o slashed.ges.o slashed. , Klaus Peter, H.o slashed.rsholm, Denmark Bech Sommer, Michael, Bagsvaerd, Denmark
PATENT ASSIGNEE(S):	H. Lundbeck A/S, Valby-Copenhagen, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6291689	B1	20010918
APPLICATION INFO.:	US 2000-565061		20000503 (9)

RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1997-DK511, filed on 10 Nov 1997
DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Dentz, Bernard
LEGAL REPRESENTATIVE:	Darby & Darby
NUMBER OF CLAIMS:	30
EXEMPLARY CLAIM:	1,27
LINE COUNT:	447

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for the preparation of citalopram is described comprising reduction of the oxo group of a compound of formula (IV), ##STR1##

wherein R.sup.1 is CN, C.sub.1-6 alkyloxycarbonyl or C.sub.1-6 alkylaminocarbonyl, ring closure of the resulting hydroxy compound thereby obtaining the corresponding 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran, then if R.sup.1 is cyano using it directly in the next step and if R.sup.1 is C.sub.1-6 alkyloxycarbonyl or C.sub.1-6 alkylaminocarbonyl, conversion of the compound to the corresponding compound wherein R.sup.1 is a cyano; and alkylation of the resulting 5-cyano compound with 3-dimethyl-aminopropylhalogenide in basic conditions thereby obtaining citalopram.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 5 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2001:107924 USPATFULL
TITLE:	Method for the preparation of citalopram
INVENTOR(S):	Petersen, Hans, Vanl.o slashed.se, Denmark Bregnedal, Peter, Aller.o slashed.d, Denmark Bogeso, Klaus Peter, H.o slashed.rsholm, Denmark
PATENT ASSIGNEE(S):	H. Lundbeck, A/S, Valby-Copenhagen, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION: US 6258842 B1 20010710
APPLICATION INFO.: US 2000-564365 20000428 (9)
RELATED APPLN. INFO.: Continuation of Ser. No. WO 1997-DK513, filed on 11 Nov 1997
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Owens, Amelia
LEGAL REPRESENTATIVE: Darby & Darby
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 347
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for the preparation of citalopram is described comprising reaction of a compound of Formula (IV) wherein R.sup.1 is H or C.sub.1-6 alkylcarbonyl successively with a Grignard reagent of 4-halogen-fluorophenyl and a Grignard reagent of 3-halogen-N,N-dimethylpropylamine, effecting ring closure of the resulting compound of Formula (IV) and converting the resulting 1,3-dihydroisobenzofuran compound to the corresponding 5-cyano derivative, i.e. citalopram. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 6 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2001:67837 USPATFULL
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans, Vanl.o slashed.se, Denmark
PATENT ASSIGNEE(S): H. Lundbeck, A/S, Copenhagen-Valby, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6229026	B1	20010508
APPLICATION INFO.:	US 2000-479832		20000107 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 1998-DK81, filed on 8 Jul 1998

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1997-826	19970708

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Owens, Amelia
LEGAL REPRESENTATIVE: Darby & Darby
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
LINE COUNT: 483
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for the preparation of citalopram comprising the steps of reacting a compound of Formula (IV) wherein R.sup.1 is C.sub.1-6 alkyl and X is O or NH, successively with a Grignard reagent of 4-halogen-fluorophenyl and a Grignard reagent of 3-halogen-N,N-dimethylpropylamine, respectively, effecting ring-closure of the resulting compound of Formula (V) wherein R.sup.1 and X are as defined above, and converting the resulting 1,3-dihydroisobenzofuran compound to the corresponding 5-cyano derivative, i.e. citalopram.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 7 OF 10 USPATFULL on STN
ACCESSION NUMBER: 94:74207 USPATFULL
TITLE: Pharmaceutically useful (+)-1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydroiso benzofuran-5-carbonitrile and non-toxic acid addition salts thereof
INVENTOR(S): Boegesoe, Klaus P., Horsholm, Denmark
Perregaard, Jens K., J gerspris, Denmark
PATENT ASSIGNEE(S): H. Lundbeck A/S, Copenhagen-Valby, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 34712		19940830	
	US 4943590		19900724	(Original)
APPLICATION INFO.:	US 1993-122009		19930914	(8)
	US 1989-363589		19890608	(Original)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1988-14057	19880614

DOCUMENT TYPE: Reissue
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dentz, Bernard
LEGAL REPRESENTATIVE: Hueschen, Gordon W.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 12
LINE COUNT: 420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The two enantiomers of the anti-depressant drug of the formula I ##STR1## are disclosed. Methods for resolving intermediates and their .[.steroselective.]. .Iadd.stereoselective .Iaddend.conversion to a corresponding .[.enatiomer.]. .Iadd.enantiomer .Iaddend.of I are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 8 OF 10 USPATFULL on STN
ACCESSION NUMBER: 90:57818 USPATFULL
TITLE: Pharmaceutically useful (+)-1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydrosobenzofuran-5-carbonitrile and non-toxic acid addition salts thereof
INVENTOR(S): Boegesoe, Klaus P., Lyngby, Denmark
Perregaard, Jens, Jaegerspris, Denmark
PATENT ASSIGNEE(S): H. Lundbeck A/S, Copenhagen-Valby, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4943590		19900724	
APPLICATION INFO.:	US 1989-363589		19890608	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1988-14057	19880614

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Lee, Mary C.
ASSISTANT EXAMINER: Dentz, Bernard I.
LEGAL REPRESENTATIVE: Hueschen, Gordon W.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 389
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The two enantiomers of the anti-depressant drug of the formula I ##STR1## are disclosed. Methods for resolving intermediates and their steroselective conversion to a corresponding enatiomer of I are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 9 OF 10 USPATFULL on STN
ACCESSION NUMBER: 87:18836 USPATFULL
TITLE: Novel intermediate and method for its preparation
INVENTOR(S): Bogeso, Klaus P., Lyngby, Denmark
PATENT ASSIGNEE(S): H. Lundbeck A/S, Copenhagen-Valby, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4650884		19870317
APPLICATION INFO.:	US 1985-761774		19850802 (6)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1984-19963	19840806

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Torrence, Dolph H.
LEGAL REPRESENTATIVE: Hueschen, Gordon W.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1,3
LINE COUNT: 228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the novel compound of the following formula: ##STR1## as well as acid addition salts thereof, a method for the preparation of the compound of Formula I, and to the use of said novel compound in the preparation of the known antidepressant drug 1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile, or a pharmaceutically acceptable acid addition salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 10 OF 10 USPATFULL on STN
ACCESSION NUMBER: 79:4514 USPATFULL
TITLE: Anti-depressive substituted 1-dimethylaminopropyl-1-phenyl phthalans
INVENTOR(S): Bogeso, Klaus P., Kgs. Lyngby, Denmark
Toft, Anders S., Farum, Denmark
PATENT ASSIGNEE(S): Kefalas A/S, Copenhagen-Valby, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4136193		19790123

APPLICATION INFO.: US 1977-757619 19770107 (5)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1976-1486	19760114

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jiles, Henry R.
ASSISTANT EXAMINER: Dentz, Bernard
LEGAL REPRESENTATIVE: Hueschen, Gordon W.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1,13
LINE COUNT: 544
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to phthalans of the following general formula: ##STR1## wherein R.sup.1 and R.sup.2 each represents halogen, a trifluoromethyl group, a cyano group or R--CO-- wherein R is an alkyl-radical with from 1-4 C-atoms inclusive, as well as acid addition salts thereof with pharmaceutically acceptable acids.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

FILE 'MARPAT' ENTERED AT 12:55:24 ON 18 OCT 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE CONTENT: 1988-PRESENT (VOL 143 ISS 15)(20051016/ED)

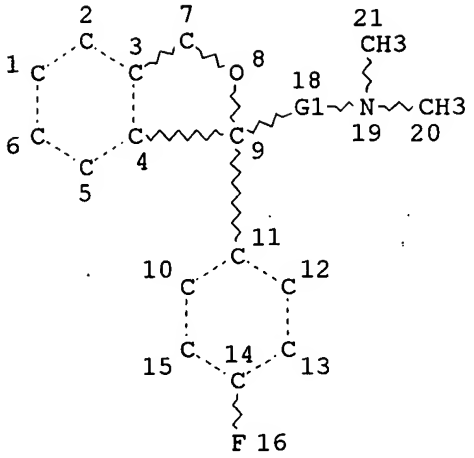
MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6916824 12 JUL 2005
DE 1020040544 28 JUL 2005
EP 1555012 20 JUL 2005
JP 2005191426 14 JUL 2005
WO 2005079855 01 SEP 2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

L13 STR



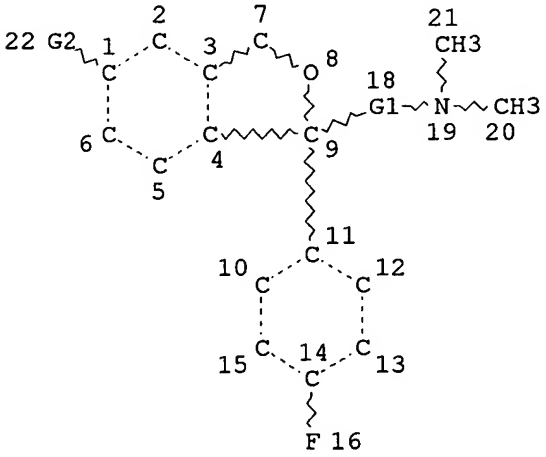
REP G1=(3-3) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L15 25 SEA FILE=MARPAT SSS FUL L13 (MODIFIED ATTRIBUTES)
L16 STR



REP G1=(3-3) CH2
VAR G2=CN/CL/BR
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L17 16 SEA FILE=MARPAT SUB=L15 SSS FUL L16 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 18 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

L17 ANSWER 1 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:56160 MARPAT
TITLE: process for purification of citalopram by hydrogenolysis halogenated isobenzofuran impurities
INVENTOR(S): Borase, Ashok Punju; Patel, Nileshkumar Sureshbai; Kilaru, Srinivasu; Thennati, Rajamannar
PATENT ASSIGNEE(S): Sun Pharmaceuticals Industries Ltd., India
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1486492	A2	20041215	EP 2004-291424	20040608
EP 1486492	A3	20050223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2005004380	A1	20050106	US 2004-865139	20040608
PRIORITY APPLN. INFO.:			IN 2003-MU602	20030610

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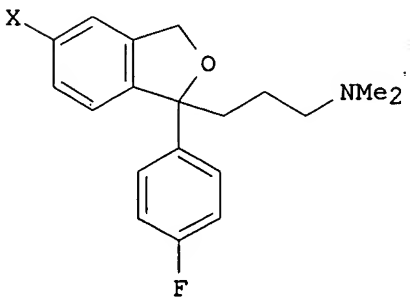

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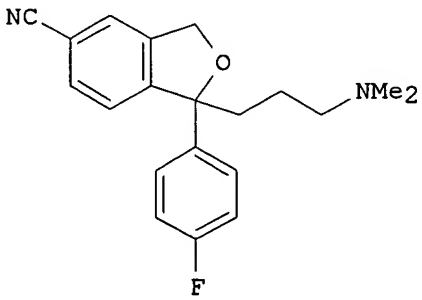


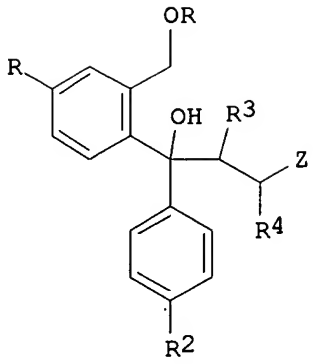
II

AB The present invention provides a process for decreasing the content of halogenated isobenzofuran impurities I (X = halo) in citalopram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalopram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

L17 ANSWER 2 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:181204 MARPAT
TITLE: Enzymic separation of intermediates for the preparation of escitalopram
INVENTOR(S): Taoka, Naoaki; Kato, Takahisa; Yamamoto, Shogo; Yoshida, Takashi; Takeda, Toshihiro; Ueda, Yasuyoshi; Petersen, Hans; Dancer, Robert; Ahmadian, Haleh; Lyngso, Lars Ole
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014821	A1	20040219	WO 2003-DK537	20030812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2495118	AA	20040219	CA 2003-2495118	20030812
EP 1534654	A1	20050601	EP 2003-783962	20030812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013114	A	20050712	BR 2003-13114	20030812
PRIORITY APPLN. INFO.:			DK 2002-1201	20020812
			US 2002-403088P	20020812
			WO 2003-DK537	20030812

GI



I

AB The (S)- or (R)-enantiomer of a diol I [R = CN or a group convertible to CN; R1 = H; R2 = halogen; R3, R4 = H; R3R4 = bond; Z = (un)substituted CH2NH2, a group convertible to CH2NMe2] and the opposite enantiomer of I [R1 = C(:W)YR5; W = O, S; Y = O, S, NH; R5 = (un)substituted alkyl, alkenyl, alkynyl] are prepared by enzymic acylation of I [R1 = H] or enzymic deacylation of I [R1 = C(:W)YR5]. Thus, I [R = CN, R, R3, R4 = H, R2 = F, Z = CH2NMe2] was treated with vinyl butyrate in the presence of Novozym 435 and pivalic acid to give (S)-I [R = CN, R, R3, R4 = H, R2 = F, Z = CH2NMe2] in 36.4% yield and 98.7% ee. (S)-I [R = CN, R, R3, R4 = H, R2 = F, Z = CH2NMe2] was converted to escitalopram oxalate of 98.5% ee.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:117333 MARPAT
TITLE: Process for the preparation of 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile via cyanation of the corresponding chloride or bromide precursors.
INVENTOR(S): Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai, Rajendran; Patel, Nileshkumar Sureshbhai
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057132	A2	20030717	WO 2003-IN6	20030107
WO 2003057132	A3	20040226		
WO 2003057132	C1	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

US 2005043550	A1	20050224	US 2004-500532	20040719
PRIORITY APPLN. INFO.:			IN 2002-MU10	20020107
			IN 2002-MU18	20020110
			IN 2002-MU847	20020930
			WO 2003-IN6	20030107

OTHER SOURCE(S): CASREACT 139:117333
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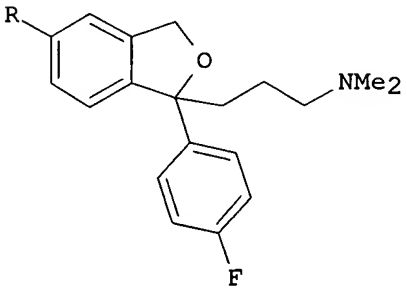

I

AB Title compound (I; R = cyano) (citalopram) was prepared by treatment of I (R = Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. The PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5 with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and 0.23% of the amide and desmethylcitalopram resp.

L17 ANSWER 4 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:73997 MARPAT
TITLE: Method for the preparation of escitalopram
INVENTOR(S): Ahmadian, Haleh; Petersen, Hans
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003051861	A1	20030626	WO 2002-DK837	20021209	
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470225	AA	20030626	CA 2002-2470225	20021209	
EP 1458701	A1	20040922	EP 2002-787443	20021209	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014327	A	20041103	BR 2002-14327	20021209	
JP 2005513069	T2	20050512	JP 2003-552745	20021209	
US 2005154051	A1	20050714	US 2003-498747	20021209	
PRIORITY APPLN. INFO.:			DK 2001-1881	20011214	
			US 2001-340450P	20011214	
			WO 2002-DK837	20021209	

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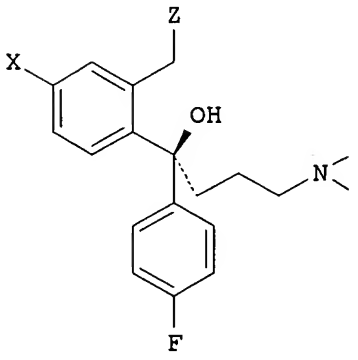

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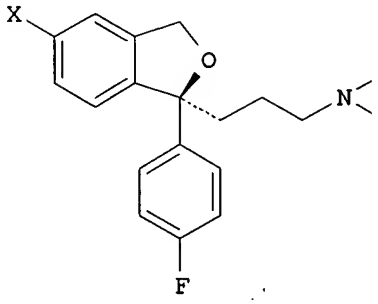

II

AB The invention relates to a method for the preparation of escitalopram by cyanation of optically active intermediates I and II, and the preparation of such intermediates by optical resolution Escitalopram was prepared by ring closure of (S,S)-enantiomer of the esters.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 16 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	138:221462 MARPAT
TITLE:	Improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide
PATENT ASSIGNEE(S):	Sekhsaria Chemicals Ltd., India
SOURCE:	Eur. Pat. Appl., 15 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288211	A1	20030305	EP 2002-255750	20020819

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: US 2001-315391P 20010828
OTHER SOURCE(S): CASREACT 138:221462
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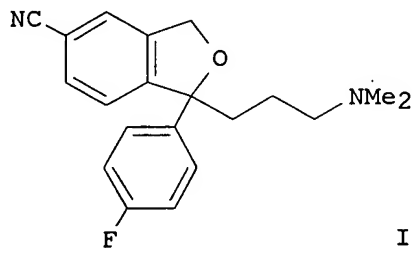

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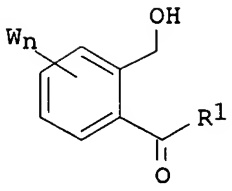
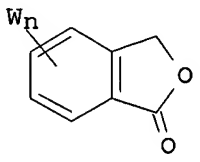


II



III

AB A process for the preparation of 1-(4'-fluorophenyl)-1-(3-dimethylamino-propyl)-5-phthalanecarbonitrile (I), or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields. Also claimed is a process for the preparation of aryl ketone II [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl, optionally containing one heteroatom; W = haloge, CN, OH, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl; n = 0 - 4] which comprises the step of reacting a phthalide III with a Grignard reagent, R1MgY (Y = halogen) and is characetrized in that the phthalide is reacted with a Lewis acid to form an adduct prior to reaction with the Grignard reagent. Thus,.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 16 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 138:55857 MARPAT
TITLE: Process for the preparation of citalopram
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: Brit. UK Pat. Appl., 11 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2376945	A1	20021231	GB 2001-15708	20010627

PRIORITY APPLN. INFO.: GB 2001-15708 20010627
OTHER SOURCE(S): CASREACT 138:55857
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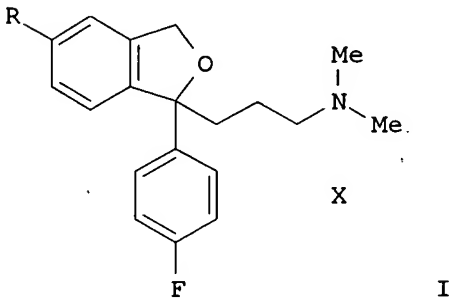

I

AB An improved process for the preparation of citalopram via substitution of the halogen of halophthalane salts I (R = halogen; X = oxalate, fumarate, maleate, citrate, acetate, formate, hydrochloride, hydrobromide, sulfate) using cuprous cyanide in an organic solvent. Thus, bromophthalane oxalate I (R = Br, X = oxalate) was reacted CuCN in diglyme under a nitrogen atmospheric at 150-155° for 3 h to form citalopram which was converted to its HBr salt I (R = CN, X = HBr).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:216863 MARPAT
TITLE: Preparation of phthalanes
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dhanmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070501	A1	20020912	WO 2002-GB1054	20020307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442613	AA	20020912	CA 2002-2442613	20020307
EP 1366034	A1	20031203	EP 2002-702553	20020307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300424	A	20031215	EE 2003-424	20020307
TR 200301444	T2	20040921	TR 2003-20030144	20020307
LT 5167	B	20041025	LT 2003-86	20030930
BG 108232	A	20050430	BG 2003-108232	20031006
LV 13132	B	20040620	LV 2003-107	20031007
ZA 2003008039	A	20041117	ZA 2003-8039	20031016
US 2004092755	A1	20040513	US 2003-471052	20031118
US 6903228	B2	20050607		
PRIORITY APPLN. INFO.:			GB 2001-5627	20010307
			WO 2002-GB1054	20020307

OTHER SOURCE(S): CASREACT 137:216863

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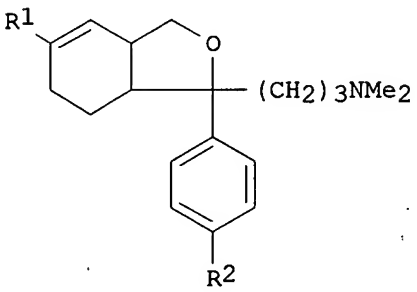

I

AB Citalopram and other phthalanes I [R1 = CN, R2 = halogen, trifluoromethyl, CN, acyl] are made by treating a salt of I [R1 = halogen] with cuprous cyanide. Thus, 100g I.oxalate [R1 = Br, R2 = F] was treated with 35 g CuCN in diglyme at 150-155° for 3 h to give 35 g I [R1 = CN, R2 = F] as the hydrobromide.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:257142 MARPAT
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068631	A1	20010920	WO 2001-DK168	20010313
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2402388	AA	20010920	CA 2001-2402388	20010313
AU 2001042298	A5	20010924	AU 2001-42298	20010313
GR 2001100123	A	20021122	GR 2001-100123	20010313
GR 1004072	B2	20021202		
EP 1265883	A1	20021218	EP 2001-915098	20010313
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TR 200202166	T2	20021223	TR 2002-20020216	20010313
BR 2001009176	A	20030422	BR 2001-9176	20010313
JP 2003527387	T2	20030916	JP 2001-567723	20010313
NZ 521201	A	20040227	NZ 2001-521201	20010313
ZA 2002006899	A	20030828	ZA 2002-6899	20020828
BG 107047	A	20030430	BG 2002-107047	20020902
NO 2002004213	A	20021113	NO 2002-4213	20020904
US 2003092919	A1	20030515	US 2002-237145	20020905
US 6762308	B2	20040713		
US 2004215025	A1	20041028	US 2004-851595	20040521

PRIORITY APPLN. INFO.:
DK 2000-401 20000313
DK 2000-415 20000314
WO 2001-DK168 20010313
US 2002-237145 20020905

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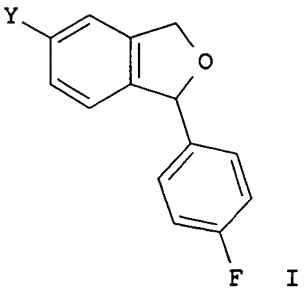

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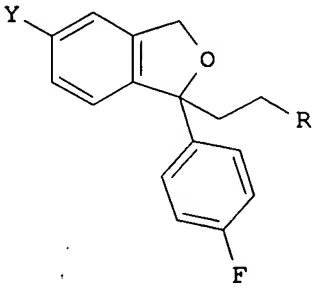

II

AB The present invention relates to a method for the preparation of

citalopram, well-known antidepressant, by alkylation of a 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran derivative I [Y = a group which may be converted to CN group] with X(CH2)2R [X = a suitable leaving group; no R group definition] to form II, followed by, in either order, conversion of the group R to a dimethylaminomethyl group and conversion of the group Y to a CN group, followed by isolation of the citalopram (no preparative data given).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:257141 MARPAT
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068630	A1	20010920	WO 2001-DK162	20010309
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2402557	AA	20010920	CA 2001-2402557	20010309
BR 2001009268	A	20021203	BR 2001-9268	20010309
EP 1265882	A1	20021218	EP 2001-913738	20010309
EP 1265882	B1	20040114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
TR 200202155	T2	20021223	TR 2002-20020215520010309	
JP 2003527386	T2	20030916	JP 2001-567722	20010309
AT 257832	E	20040115	AT 2001-913738	20010309
PT 1265882	T	20040630	PT 2001-913738	20010309
ES 2214400	T3	20040916	ES 2001-1913738	20010309
ZA 2002006897	A	20030828	ZA 2002-6897	20020828
BG 107051	A	20030530	BG 2002-107051	20020902
NO 2002004198	A	20020903	NO 2002-4198	20020903
US 2003050484	A1	20030313	US 2002-238907	20020906
US 6806376	B2	20041019		
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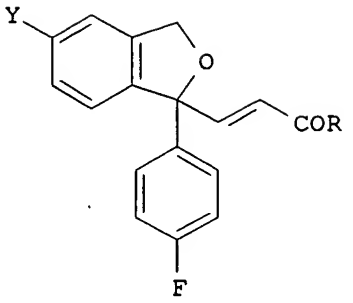

I

AB The invention relates to a method for the preparation of citalopram, well-known antidepressant, comprising, in either order, subjecting a compound I [Y = CN or a group which may be converted to CN group; R = H, OR1, NH2, NHMe, NMe2 (R1 = H, alkyl, alkenyl, alkynyl, (un)substituted aryl or aralkyl)] to reduction of the double bond in the side chain of formula -CH=CH-COR followed by conversion of the group -COR or its reduced form to a dimethylaminomethyl group; and then if Y is not cyano, conversion of the group Y to a cyano group; followed by isolation of citalopram base or a pharmaceutically acceptable acid addition salt thereof (preparative data were not given). Preparation of compound I is also claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:257140 MARPAT
TITLE: Stepwise alkylation of 5-substituted 1-(4-fluorophenyl)-1,3-dihydroisobenzofurans (citalopram intermediates)
INVENTOR(S): Petersen, Hans; Ahmadian, Haleh
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068629	A1	20010920	WO 2001-DK159	20010309
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402553	AA	20010920	CA 2001-2402553	20010309
EP 1265881	A1	20021218	EP 2001-913735	20010309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
TR 200202195	T2	20021223	TR 2002-20020219	20010309
BR 2001009364	A	20021224	BR 2001-9364	20010309
JP 2003527385	T2	20030916	JP 2001-567721	20010309
NZ 521204	A	20040326	NZ 2001-521204	20010309
BG 107046	A	20030530	BG 2002-107046	20020902
ZA 2002007024	A	20030902	ZA 2002-7024	20020902
US 2003083509	A1	20030501	US 2002-242804	20020910
US 6864379	B2	20050308		
NO 2002004352	A	20021008	NO 2002-4352	20020912
US 2005020670	A1	20050127	US 2004-917667	20040813
PRIORITY APPLN. INFO.:			DK 2000-403	20000313
			DK 2000-414	20000314
			WO 2001-DK159	20010309
			US 2002-242804	20020910

OTHER SOURCE(S): CASREACT 135:257140

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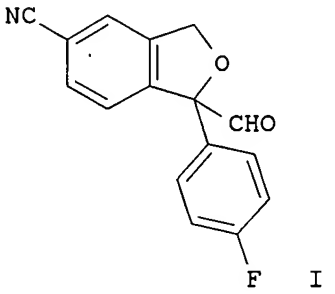

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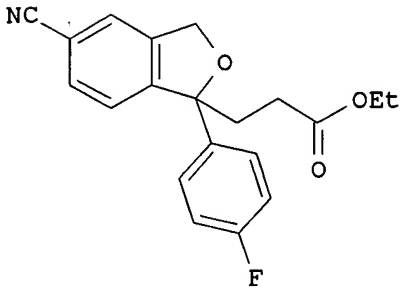

II

AB Methods for manufacture of citalopram, well-known antidepressant, through stepwise alkylation of 5-R-substituted 1-(4-fluorophenyl)-1,3-dihydroisobenzofurans [R = CN, OH, NH2, etc.] are disclosed. Thus, reacting 1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile with Me formate in the presence of LDA in THF followed by reacting the resulting 1-formyl intermediate I with tri-Et phosphonoacetate in the presence of LDA in THF, hydrogenation of the crude intermediate, and reacting the intermediate II with Me chloroaluminum dimethylamide in PhMe afforded citalopram.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 16 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 135:137393 MARPAT
Correction of: 134:353251

TITLE: Method for the preparation of citalopram

INVENTOR(S): Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S): H Lundbeck A/S, Den.

SOURCE: Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

GB 2354240	A1	20010321	GB 2001-1508	19991119
GB 2354240	B2	20010523		
IT 99MI1579	A1	20010115	IT 1999-MI1579	19990715
WO 2000011926	A2	20000309	WO 1999-DK643	19991119
WO 2000011926	A3	20000629		

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1105382	A2	20010613	EP 1999-968206	19991119
EP 1105382	B1	20020213		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

DE 19983486	T	20011018	DE 1999-19983486	19991119
DE 19983486	C2	20020905		
AT 213237	E	20020215	AT 1999-968206	19991119
BR 9917367	A	20020305	BR 1999-17367	19991119
AT 9909040	A	20020515	AT 1999-9040	19991119
AT 409960	B	20021227		
TR 200103700	T2	20020521	TR 2001-200103700	19991119
JP 2002523432	T2	20020730	JP 2000-567065	19991119
JP 3389571	B2	20030324		
PT 1105382	T	20020731	PT 1999-968206	19991119
ES 2172356	T3	20020916	ES 1999-968206	19991119
CZ 292174	B6	20030813	CZ 2001-319	19991119
CN 1129593	B	20031203	CN 1999-816768	19991119
NZ 514982	A	20040130	NZ 1999-514982	19991119
CA 2290125	C	20040810	CA 1999-2290125	19991122
CA 2290125	AA	20001225		
NO 2001000318	A	20010220	NO 2001-318	20010119
SE 2001000194	A	20010425	SE 2001-194	20010124
SE 516689	C2	20020212		
FI 2001000154	A	20010209	FI 2001-154	20010125
FI 108538	B1	20020215		
ZA 2001007956	A	20020927	ZA 2001-7956	20010927
ZA 2001008855	A	20020611	ZA 2001-8855	20011026
US 2002061925	A1	20020523	US 2001-12025	20011106
US 6750358	B2	20040615		
BG 106190	A	20020830	BG 2001-106190	20011207
ZA 2002005023	A	20030623	ZA 2002-5023	20020621
HK 1047745	A1	20040910	HK 2002-109330	20021224

PRIORITY APPLN. INFO.: DK 1999-921 19990625
WO 1999-DK643 19991119

OTHER SOURCE(S): CASREACT 135:137393

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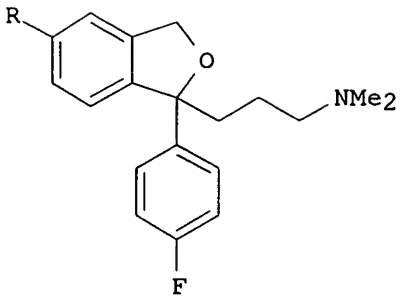

I

AB A method for preparing the antidepressant, citalopram [I; R = CN], by reacting an isobenzofuranpropanamine [I; R = Cl or Br] with a cyanide source in the presence of a nickel catalyst is presented. Citalopram is produced in high yield as a very pure product using this catalytic process. Thus, sequential addition of I (R = Cl) and NaCN to the Ni catalyst formed by reflux of NiCl2 with PPh3 in AcCN in the presence of a catalytic amount of Zn, followed by workup and treatment with oxalic acid, gave citalopram oxalate in 55% yield.

L17 ANSWER 12 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:61225 MARPAT
TITLE: Process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation
INVENTOR(S): Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico
PATENT ASSIGNEE(S): H. Lundbeck A/s, Den.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047877	A2	20010705	WO 2001-DK148	20010307
WO 2001047877	A3	20001227		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2359810	AA	20010705	CA 2001-2359810	20010307
CA 2359810	C	20021105		
AU 2001039202	A5	20010709	AU 2001-39202	20010307
EP 1181272	A2	20020227	EP 2001-913727	20010307
EP 1181272	B1	20020828		
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BR 2001006271	A	20020521	BR 2001-6271	20010307
TR 200200018	T1	20020621	TR 2002-20020001	20010307
AT 222899	E	20020915	AT 2001-913727	20010307
PT 1181272	T	20030131	PT 2001-913727	20010307
ES 2181663	T3	20030301	ES 2001-1913727	20010307
JP 2003519121	T2	20030617	JP 2001-549350	20010307
SK 284418	B6	20050401	SK 2001-1847	20010307
NL 1017534	C1	20010426	NL 2001-1017534	20010308
DK 200100386	A5	20020629	DK 2001-386	20010308
GB 2356199	A1	20010516	GB 2001-5981	20010312
GB 2356199	B2	20011003		
CZ 293140	B6	20040218	CZ 2001-891	20010312
FI 108640	B1	20020228	FI 2001-501	20010313
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CH 691536	A	20010815	CH 2001-546	20010322
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FR 2818977	A1	20020705	FR 2001-4025	20010326
FR 2818977	B1	20031205		
NL 1018410	C1	20011113	NL 2001-1018410	20010628
BE 1013316	A6	20011106	BE 2001-466	20010709
GB 2361697	A1	20011031	GB 2001-17095	20010713
CH 691999	A	20010726	CH 2001-1412	20010726
ES 2170733	A1	20020801	ES 2001-1763	20010727
ES 2170733	B1	20031216		
AU 750006	B1	20020711	AU 2001-65478	20010827
SE 2001003044	A	20020629	SE 2001-3044	20010914
ZA 2001010133	A	20030113	ZA 2001-10133	20011210
BG 106219	A	20020830	BG 2001-106219	20011213
US 2002087012	A1	20020704	US 2001-35005	20011220
US 6855834	B2	20050215		
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HR 2002000005	A1	20030430	HR 2002-5	20020104
US 2003178295	A1	20030925	US 2003-361800	20030210
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OTHER SOURCE(S): CASREACT 135:61225
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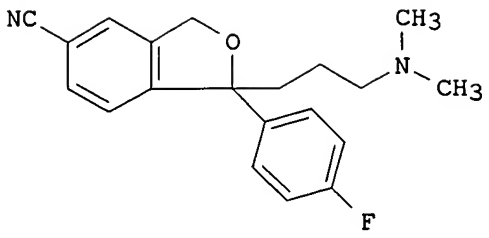

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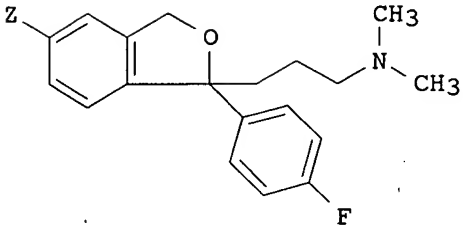

II

AB High-purity citalopram (I) is prepared on an industrial scale by: subjecting a citalopram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalopram product is optionally subjected to some initial purification and the crude citalopram base is subsequently subjected to a thin- or falling-film distillation process.

L17 ANSWER 13 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:61224 MARPAT
TITLE: Method for the preparation and purification of citalopram
INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045483	A2	20010628	WO 2001-DK147	20010307
WO 2001045483	A3	20011227		

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NL 1017525	C1	20010426	NL 2001-1017525	20010307	
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EP 1181713	A2	20020227	EP 2001-913726	20010307	
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TR 200201166	T1	20021021	TR 2002-20020116	20010307
JP 2003517484	T2	20030527	JP 2001-546230	20010307
BR 2001006272	A	20040615	BR 2001-6272	20010307
EP 1462447	A2	20040929	EP 2004-4482	20010307
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AT 277920	E	20041015	AT 2001-913726	20010307
PT 1181713	T	20050228	PT 2001-913726	20010307
SK 284428	B6	20050401	SK 2001-1848	20010307
ES 2228824	T3	20050416	ES 2001-1913726	20010307
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GB 2359811	B2	20030305		
CZ 292200	B6	20030813	CZ 2001-890	20010312
FI 108639	B1	20020228	FI 2001-500	20010313
NO 312462	B1	20020513	NO 2001-1271	20010313
FR 2812877	A1	20020215	FR 2001-3455	20010314
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GR 1003874	B1	20020424	GR 2001-100132	20010316
DE 10112829	C1	20020725	DE 2001-10112829	20010316
CH 691535	A	20010815	CH 2001-545	20010322
BE 1013212	A6	20011002	BE 2001-188	20010322
NL 1018360	C1	20011004	NL 2001-1018360	20010622
BE 1013213	A6	20011002	BE 2001-435	20010626
CH 691998	A	20011231	CH 2001-1411	20010726
ES 2170732	A1	20020801	ES 2001-1762	20010727
AU 744112	B1	20020214	AU 2001-65477	20010827
SE 517623	C2	20020625	SE 2001-3045	20010914
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BG 106203	A	20020830	BG 2001-106203	20011210
ZA 2001010179	A	20021211	ZA 2001-10179	20011211
NZ 516298	A	20021220	NZ 2001-516298	20011220
HR 2002000004	A1	20030430	HR 2002-4	20020104
US 2002120005	A1	20020829	US 2002-46126	20020108
US 6455710	B2	20020924		

PRIORITY APPLN. INFO.:	DK 2000-1929	20001222
	NL 2001-1017525	20001222
	EP 2001-913726	20010307
	WO 2001-DK147	20010307
	GB 2001-5983	20010312
	CH 2001-545	20010322

OTHER SOURCE(S): CASREACT 135:61224
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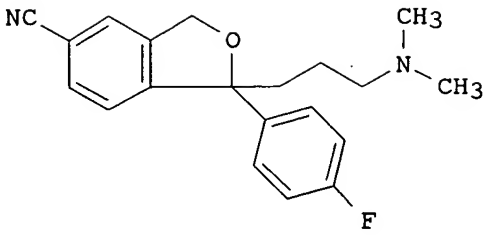
Searcher : Shears 571-272-2528



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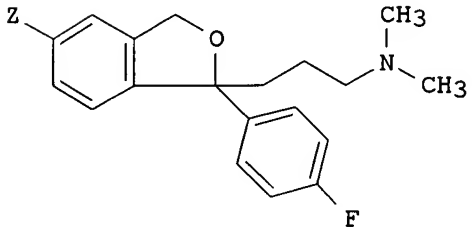

II

AB A process for the preparation and purification of citalopram (I) is presented in
which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization and recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

L17 ANSWER 14 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:353251 MARPAT
TITLE: Method for the preparation of citalopram by nickel-catalyzed cyanation of halo precursors
INVENTOR(S): Petersen, Hans; Rock, Michael Harold
PATENT ASSIGNEE(S): H Lundbeck A/S, Den.
SOURCE: Brit. UK Pat. Appl., 16 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2354240 A1		20010321	GB 2001-1508	19991119
PRIORITY APPLN. INFO.:			DK 1999-921	19990625
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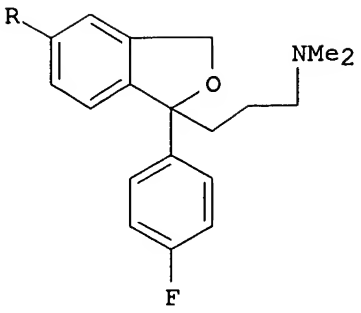

I

AB A method for the preparation of citalopram is presented, comprising the reaction of isobenzofuranpropanamine I, wherein R is Cl or Br, with a cyanide source in the presence of a nickel catalyst and isolation of the corresponding 5-cyano compound, i.e. citalopram.

L17 ANSWER 15 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:194283 MARPAT
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans; Rock, Michael Harold; Svane, Henrik
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000013648	A2	20000316	WO 1999-DK640	19991122
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IT 99MI1581	A1	20010115	IT 1999-MI1581	19990715
ES 2169709	A1	20020701	ES 2001-50056	19991025
JP 2003012663	A2	20030115	JP 2002-106016	19991025
EP 1298124	A1	20030402	EP 2002-28326	19991025
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AU 2000013745	A5	20000327	AU 2000-13745	19991122
CA 2290127	AA	20001225	CA 1999-2290127	19991122
CA 2290127	C	20050125		
CA 2475401	AA	20001225	CA 1999-2475401	19991122
GB 2354239	A1	20010321	GB 2001-1504	19991122
GB 2354239	B2	20010606		

GB 2357761	A1	20010704	GB 2001-5182	19991122
GB 2357761	B2	20010905		
EP 1159274	A2	20011205	EP 1999-968622	19991122
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BR 9917368	A	20020305	BR 1999-17368	19991122
AT 9909041	A	20020515	AT 1999-9041	19991122
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DE 19983487	C1	20020725	DE 1999-19983487	19991122
JP 2002526386	T2	20020820	JP 2000-568457	19991122
JP 3447267	B2	20030916		
AT 235478	E	20030415	AT 1999-968622	19991122
ES 2189699	A1	20030701	ES 2001-50011	19991122
CZ 292198	B6	20030813	CZ 2001-320	19991122
PT 1159274	T	20030829	PT 1999-968622	19991122
ES 2194545	T3	20031116	ES 1999-968622	19991122
NZ 514979	A	20040130	NZ 1999-514979	19991122
CN 1502616	A	20040609	CN 2003-10118780	19991122
SE 2001000193	A	20010425	SE 2001-193	20010124
SE 516690	C2	20020212		
FI 2001000155	A	20010209	FI 2001-155	20010125
FI 108641	B1	20020228		
ZA 2001008854	A	20020611	ZA 2001-8854	20011026
US 2002077353	A1	20020620	US 2001-12054	20011106
BG 106191	A	20020830	BG 2001-106191	20011207
HK 1049002	A1	20041231	HK 2003-101234	20030218
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			EP 1999-950511	19991025
			JP 2000-571018	19991025
			CA 1999-2290127	19991122
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OTHER SOURCE(S): CASREACT 132:194283

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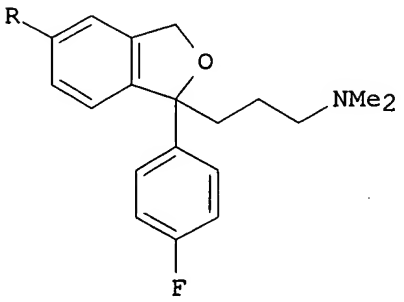

I

AB The title compound [I; R = CN], the well known antidepressant (no data), was prepared by reacting a compound I [wherein R = halo, CF3(CF2)nSO2; n = 0-8] with a cyanide source in the presence of a palladium catalyst and a catalytic amount of Cu+ or Zn2+, or with Zn(CN)2 in the presence of a palladium catalyst.

L17 ANSWER 16 OF 16 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 117:917 MARPAT
TITLE: Use of 1-(3-(dimethylamino)propyl)-1-phenylphthalans derivatives for the treatment of cerebrovascular disorders
INVENTOR(S): Tanaka, Yoshiaki; Kobayashi, Naomi; Kurimoto, Tadashi; Ikeda, Yugo
PATENT ASSIGNEE(S): Lundbeck, H., A/S, Den.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 474580	A2	19920311	EP 1991-610063	19910816
EP 474580	A3	19920603		
EP 474580	B1	19940928		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
IL 98968	A1	19960618	IL 1991-98968	19910725
ZA 9106187	A	19920429	ZA 1991-6187	19910806
CA 2049368	AA	19920307	CA 1991-2049368	19910816
CA 2049368	C	20011023		
KR 9702246	B1	19970226	KR 1991-14255	19910819
AU 9182594	A1	19920312	AU 1991-82594	19910820
AU 644204	B2	19931202		
JP 04244024	A2	19920901	JP 1991-224192	19910904
JP 08005787	B4	19960124		
US 5296507	A	19940322	US 1993-1571	19930106
PRIORITY APPLN. INFO.:			DK 1990-2132	19900906
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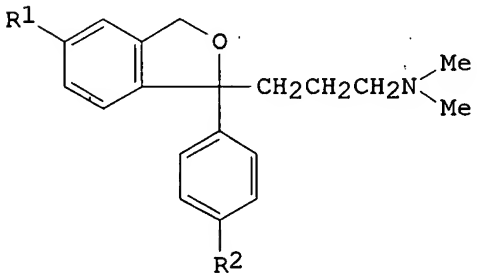

I

AB The title compds. [I; R1, R2 = halo, CF3, cyano, RCO (R = alkyl)] or acid addition salts thereof are useful in the treatment of dementia, cerebrovascular disorders, and for inhibiting platelet aggregation. Citalopram (II) (40mg/kg) was i.p. injected into gerbils 30 min before carotid occlusion (5 min); 7 days later the animals were killed and surviving neurons were counted. The number of surviving neurons was 95.8 as compared to 12.8/mm for controls. An injection solution contained II 10, sorbitol 42.9, acetic acid 0.63, NaOH 22 mg, and water 1mL.

FILE 'MARPATPREV' ENTERED AT 12:59:28 ON 18 OCT 2005

FILE COVERS CURRENT RECORDS AND IS UPDATED DAILY
FILE LAST UPDATED: 18 OCT 2005(20051018)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6797117 28 SEP 2004
DE 10322109 4 MAY 2004
EP 1491180 29 DEC 2004
JP 2004196848 15 JUL 2004
WO 2005079855 1 SEP 2005

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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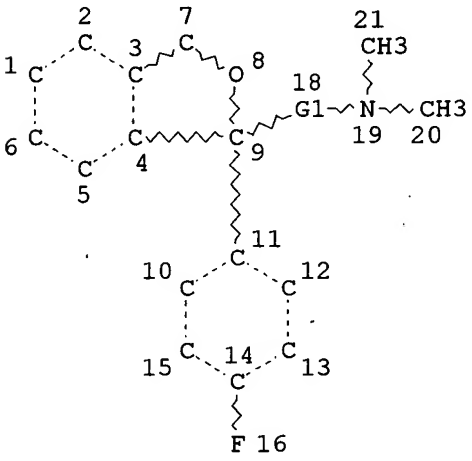

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

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Searcher : Shears 571-272-2528

FILE 'CASREACT' ENTERED AT 13:01:04 ON 18 OCT 2005

FILE CONTENT:1840 - 16 Oct 2005 VOL 143 ISS 16

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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* CASREACT now has more than 9.2 million reactions
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Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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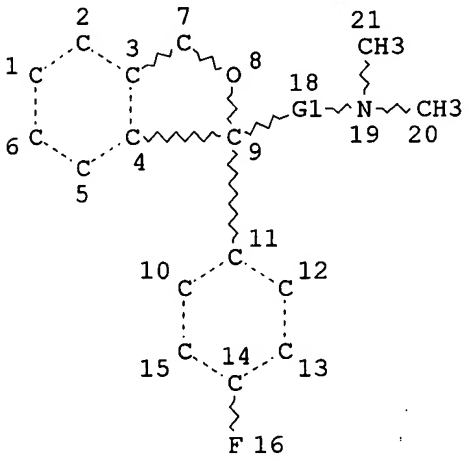

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NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
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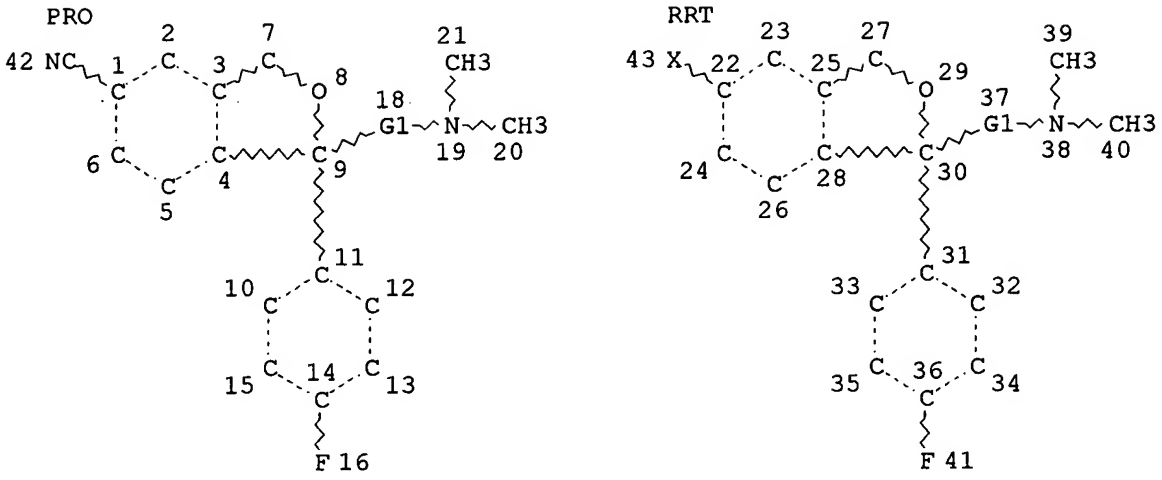
Searcher : Shears 571-272-2528



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SEARCH TIME: 00.00.01

L29 ANSWER 1 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:157024 CASREACT
TITLE: A processes for preparation of escitalopram, useful as antidepressant
INVENTOR(S): Nannapaneni, Venkaiah Chowdary; Muddasani, Pulla Reddy; Talasila, Sambashiva Rao; Nekkanti, Srinivasa Rao; Podile, Khadgapathi
PATENT ASSIGNEE(S): Natco Pharma Limited, India
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065375	A1	20040805	WO 2003-IN220	20030617

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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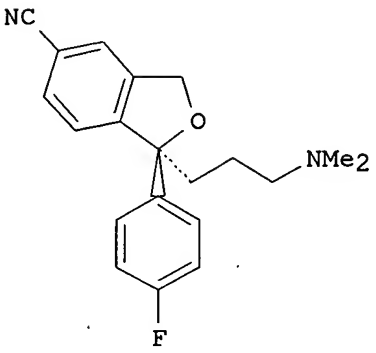

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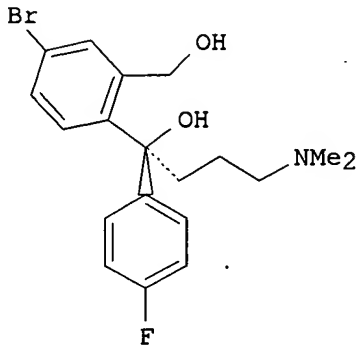
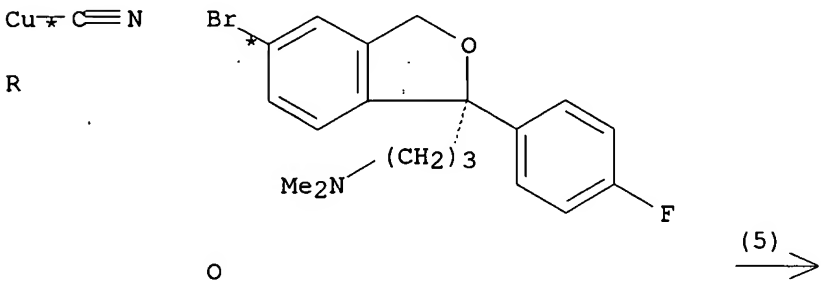
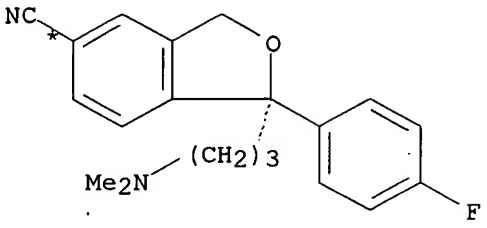


II

AB The present invention relates to an improved process for the preparation of escitalopram (I) which consist of a sequential double Grignard reaction on 5-bromophthalide, isolation of di-magnesium salt, neutralization of di-magnesium salt, resolution of dihydroxy compound of the formula II, cyclization, and cyanation. The proposed process utilizes the insol. property of di-magnesium salt in a mixture of THF and a non-polar organic solvent, and separates it from impurities by simple filtration thereby making the isolation and purification process simple. Advantages of the proposed process include (a) high yield preparation of escitalopram (>25%), (b) escitalopram can be prepared in a simple and easy to adopt manner without involving any purification steps, (c) the process produces pure (>98%) di-magnesium salt of intermediate compound was isolated, etc.

RX(5) OF 24 ...R + O ===> S





S
YIELD 70%

RX(5) RCT R 544-92-3, O **488148-14-7**

STAGE(1)
SOL 68-12-2 DMF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 150 deg C
SUBSTAGE(3) 8 hours, 145 - 150 deg C
SUBSTAGE(4) 150 deg C -> 30 deg C

STAGE(2)
SOL 7732-18-5 Water

PRO S **128196-01-0**
NTE thermal
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

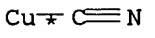
L29 ANSWER 2 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:357194 CASREACT
TITLE: Process for the manufacture of citalopram hydrobromide from 5-bromophthalide
INVENTOR(S): Chodankar, Nandkumar; Bhobe, Ajit; Oak, G. M.; Eappan, Philip
PATENT ASSIGNEE(S): Sekhsaria Chemicals Limited, India
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004077870	A1	20040422	US 2002-277451	20021022
US 6812355	B2	20041102		
PRIORITY APPLN. INFO.:			US 2002-277451	20021022

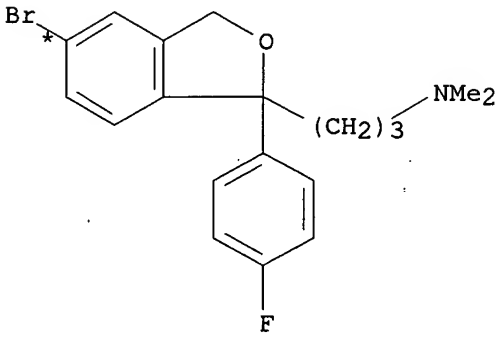
OTHER SOURCE(S): MARPAT 140:357194
AB Disclosed is a process for the preparation of 1-(4-fluorophenyl)-1-(3-dimethylamino-propyl)-5-phthalanecarbonitrile (citalopram) (known antidepressant) or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide using p-fluorobromobenzene and then

N,N-dimethylaminopropylmagnesium chloride, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields.

RX(4) OF 10 ...P + **M** ===> **Q**

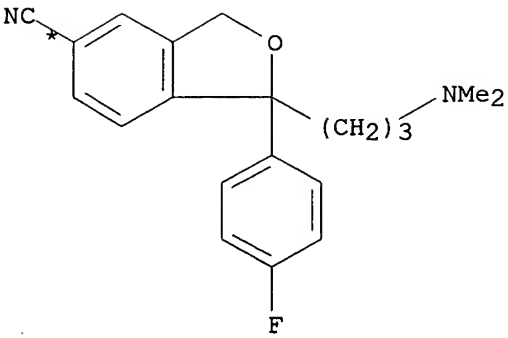


P



M

(4) →



Q

RX(4) RCT P 544-92-3, M **64169-39-7**
RGT R 50-99-7 D-Glucose, S 7681-11-0 KI
PRO Q **59729-33-8**
SOL 68-12-2 DMF
CON 140 - 160 deg C
NTE thermal

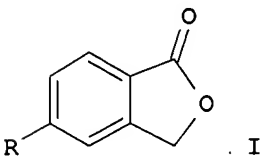
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searcher : Shears 571-272-2528

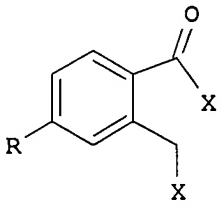
L29 ANSWER 3 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:145992 CASREACT
TITLE: Process for the preparation of 1-(3-dimethylaminopropyl)-1-(4-fluorophenyl) -1,3-dihydroisobenzofuran-5-carbonitrile
INVENTOR(S): Hilden, Leif; Rummakko, Petteri; Grumann, Arne; Pietikaeinen, Pekka
PATENT ASSIGNEE(S): Orion Corporation Fermion, Finland
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011450	A1	20040205	WO 2003-FI557	20030710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005209467	A1	20050922	US 2005-45087	20050131
PRIORITY APPLN. INFO.:			FI 2002-1421	20020730
			US 2002-419150P	20021018
			WO 2003-FI557	20030710

OTHER SOURCE(S): MARPAT 140:145992
GI



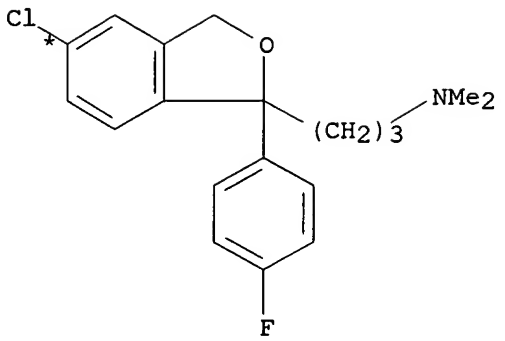
I



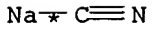
II

AB The present invention is directed to novel processes for the preparation of citalopram comprising halogenation of a phthalides I (wherein R is a suitable group to be changed to CN) to afford an acid halides II (X is halogen) and thereafter obtaining citalopram through two successive reactions with suitable organometallic halides or organoboranes or by a reaction with organometallic 4-fluorophenylhalide or 4-fluorophenylborane followed by reduction and alkylation, and an exchange of R to cyano to afford citalopram. The order of the reactions can be varied depending e.g. on the starting compound used.

RX(3) OF 9 ...**I** + M ===> **N**

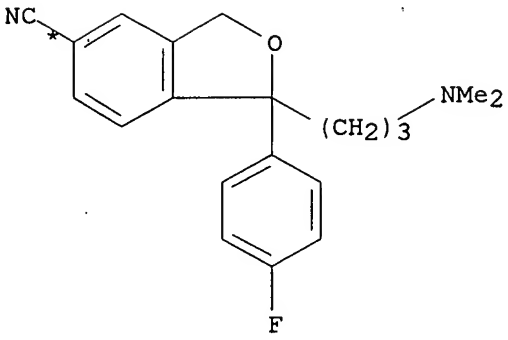


I



M

(3)



N

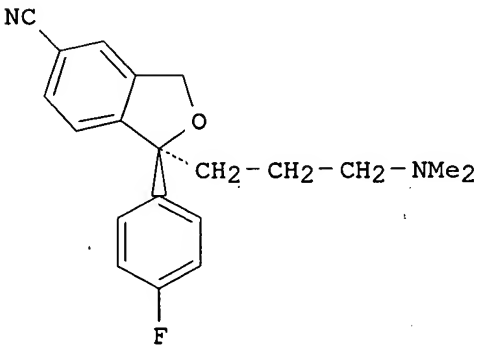
RX(3) RCT I **64169-45-5**, M 143-33-9
RGT O 7440-66-6 Zn
PRO N **59729-33-8**
CAT 603-35-0 PPh3, 7718-54-9 NiCl2
SOL 75-05-8 MeCN
CON 15 hours, reflux
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:337880 CASREACT
TITLE: Preparation of escitalopram via the chiral enriched diol monoesters of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol
INVENTOR(S): Tse, Hoi Lun Allan
PATENT ASSIGNEE(S): Torcan Chemical Ltd., Can.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

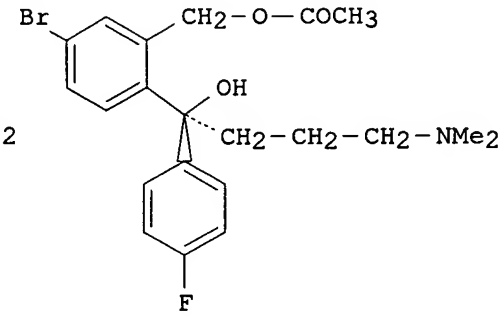
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087081	A1	20031023	WO 2003-CA522	20030408
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2381341	AA	20031009	CA 2002-2381341	20020409
EP 1495013	A1	20050112	EP 2003-711761	20030408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			CA 2002-2381341	20020409
			WO 2003-CA522	20030408

GI



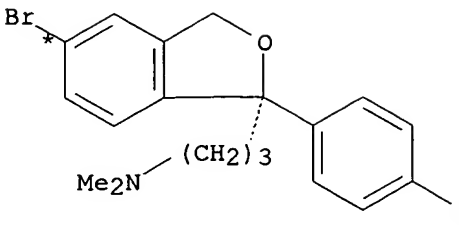
I



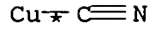
II

AB Preparation of escitalopram (I) via the chiral enriched monoacetate ester of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol (II) was disclosed. For example, a racemic mixture of monoacetate ester II (13.52 g) and (+)-di-p-toluoyl tartaric acid (11.92 g) in acetone (135 mL) was heated at reflux until a pale brown solution was obtained. The solution was cooled, the acetone removed under vacuum and the resulting brown foam recrystd. from acetone-hexane (2:1) to afford the (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II with a diastereomeric ratio of 97:3. Of note, the claimed (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II was converted to escitalopram oxalate in 4-steps with [α]D = +10.1° (at 20°C, c 0.95 in MeOH).

RX(8) OF 36 ...W + Y ===> Z

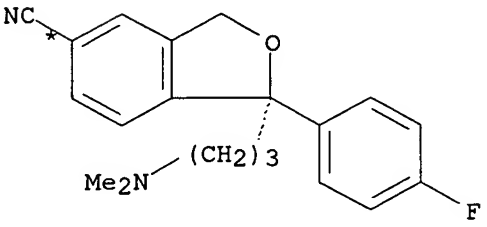


W



Y

(8) →



Z
YIELD 60%

RX(8) RCT W **488148-14-7**, Y 544-92-3
PRO Z **128196-01-0**
SOL 127-19-5 AcNMe2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 150 deg C
SUBSTAGE(3) 21 hours, 150 deg C
NTE thermal
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 5 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:117333 CASREACT
TITLE: Process for the preparation of 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile via cyanation of the corresponding chloride or bromide precursors.
INVENTOR(S): Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai, Rajendran; Patel, Nileshkumar Sureshbhai
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057132	A2	20030717	WO 2003-IN6	20030107
WO 2003057132	A3	20040226		
WO 2003057132	C1	20040415		

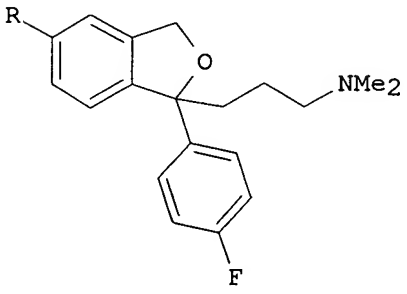
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005043550	A1	20050224	US 2004-500532	20040719
PRIORITY APPLN. INFO.:			IN 2002-MU10	20020107
			IN 2002-MU18	20020110
			IN 2002-MU847	20020930
			WO 2003-IN6	20030107

OTHER SOURCE(S): MARPAT 139:117333

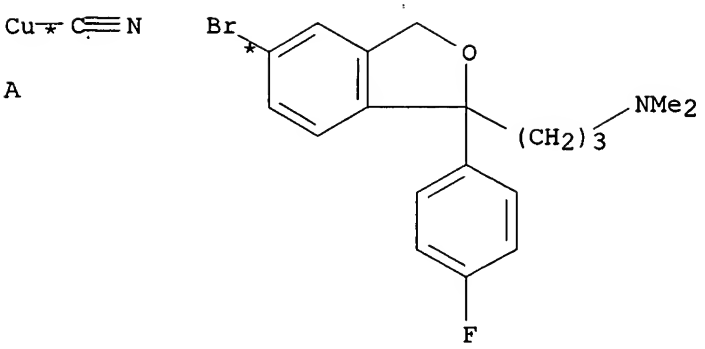
GI



I

AB Title compound (I; R = cyano) (citalopram) was prepared by treatment of I (R = Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. The PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5 with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and 0.23% of the amide and desmethylcitalopram resp.

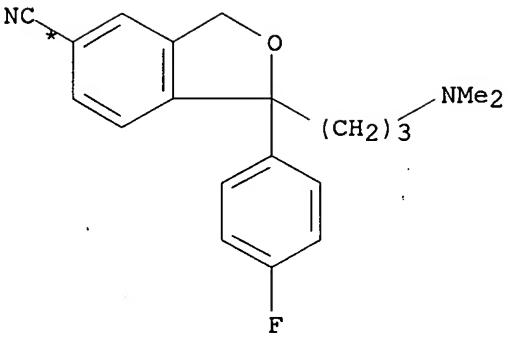
RX(1) OF 2 A + **B** ===> **C**



A

B

(1) →



C

RX(1) RCT A 544-92-3, B **64169-39-7**

STAGE(1)
RGT D 7681-11-0 KI
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 145 deg C
SUBSTAGE(3) 28 hours, 135 - 145 deg C
SUBSTAGE(4) 145 deg C -> 100 deg C

STAGE(2)
RGT E 7664-41-7 NH3
SOL 108-88-3 PhMe
CON SUBSTAGE(2) 2 hours

PRO C **59729-33-8**
NTE optimization study

L29 ANSWER 6 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:305791 CASREACT
TITLE: Process for the preparation of citalopram, and intermediates and derivatives

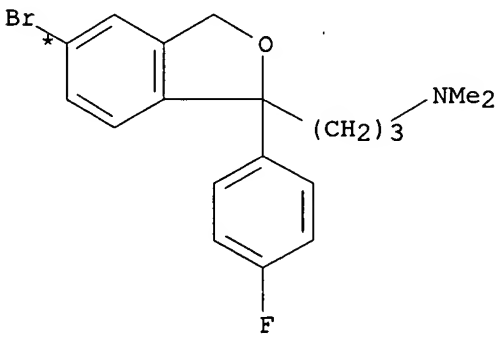
Searcher : Shears 571-272-2528

INVENTOR(S): Malik, A. Aslam; Palandoken, Hasan; Stringer, Joy A.; Huang, Dershing; Romero, Antonio; Dapremont, Olivier
PATENT ASSIGNEE(S): Pharmachem Technologies Limited, UK
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

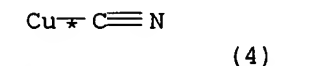
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029236	A1	20030410	WO 2002-EP10645	20020923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003153774	A1	20030814	US 2002-242322	20020911
CA 2461213	AA	20030410	CA 2002-2461213	20020923
EP 1430044	A1	20040623	EP 2002-779403	20020923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1556800	A	20041222	CN 2002-818642	20020923
JP 2005507900	T2	20050324	JP 2003-532485	20020923
NO 2004001200	A	20040323	NO 2004-1200	20040323
ZA 2004002273	A	20050323	ZA 2004-2273	20040323
PRIORITY APPLN. INFO.:			US 2001-324821P	20010924
			US 2002-242322	20020911
			WO 2002-EP10645	20020923

AB The present invention provides a process for the preparation of Citalopram, a known antidepressant.

RX(4) OF 7 ...J + M ===> N



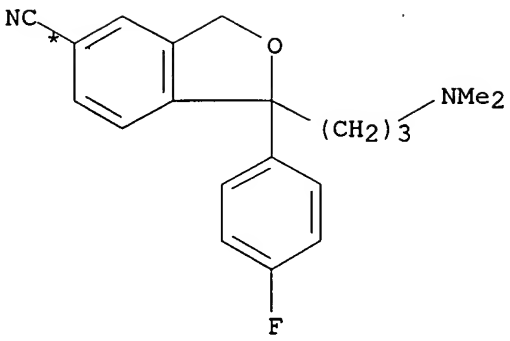
J



M

(4) →

Searcher : Shears 571-272-2528



N
YIELD 84%

RX(4) RCT J **64169-39-7**, M 544-92-3

STAGE(1)
RGT O 143-33-9 NaCN
SOL 108-88-3 PhMe, 68-12-2 DMF
CON SUBSTAGE(1) room temperature -> 159 deg C
SUBSTAGE(2) 159 deg C -> 70 deg C

STAGE(2)
RGT O 143-33-9 NaCN
SOL 7732-18-5 Water

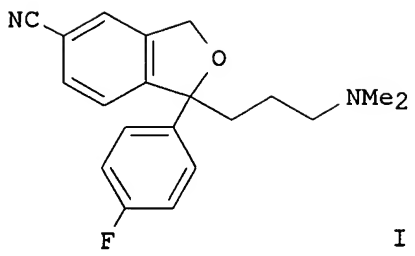
PRO N **59729-33-8**
NTE thermal
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 7 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:221462 CASREACT
TITLE: Improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide
PATENT ASSIGNEE(S): Sekhsaria Chemicals Ltd., India
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

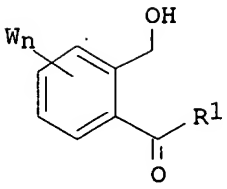
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288211	A1	20030305	EP 2002-255750	20020819

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

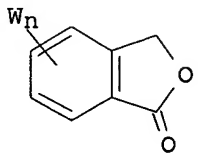
PRIORITY APPLN. INFO.: US 2001-315391P 20010828
OTHER SOURCE(S): MARPAT 138:221462
GI



I



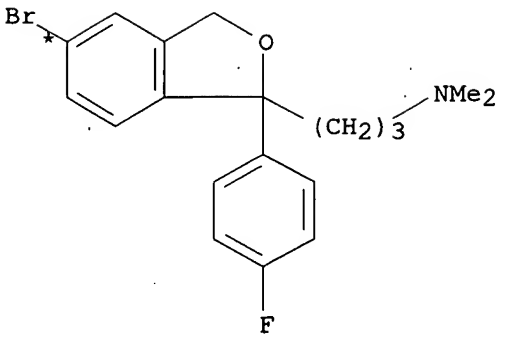
II



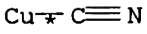
III

AB A process for the preparation of 1-(4'-fluorophenyl)-1-(3-dimethylamino-propyl)-5-phthalanecarbonitrile (I), or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields. Also claimed is a process for the preparation of aryl ketone II [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl, optionally containing one heteroatom; W = haloge, CN, OH, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl; n = 0 - 4] which comprises the step of reacting a phthalide III with a Grignard reagent, R1MgY (Y = halogen) and is characetrized in that the phthalide is reacted with a Lewis acid to form an adduct prior to reaction with the Grignard reagent. Thus,.

RX(1) OF 9 ...**A** + B ===> **C**



A



B

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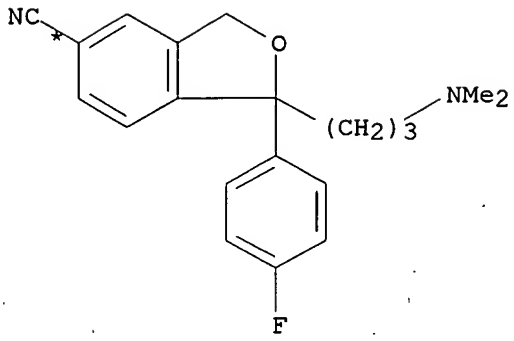


● HBr

C

RX(1) RCT A **64169-39-7**, B 544-92-3

STAGE(1)
RGT D 7681-11-0 KI
SOL 68-12-2 DMF
CON 140 - 160 deg C

STAGE(2)
RGT E 1336-21-6 NH4OH
SOL 7732-18-5 Water, 108-88-3 PhMe
CON SUBSTAGE(1) 50 deg C
SUBSTAGE(2) 20 deg C

STAGE(3)
RGT F 64-18-6 HCO2H
SOL 7732-18-5 Water
CON SUBSTAGE(1) 30 - 35 deg C, pH 5.4 - 5.5
SUBSTAGE(2) 0 - 5 deg C, pH 5.4 - 5.5

Searcher : Shears 571-272-2528

PRO C **59729-32-7**
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 8 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:122548 CASREACT
TITLE: Method for the preparation of escitalopram via chromatographic resolution of citalopram or its intermediates using carbohydrate-based chiral stationary phases
INVENTOR(S): Bech Sommer, Michael; Nielsen, Ole; Petersen, Hans; Ahmadian, Haleh; Pedersen, Henrik; Brosen, Peter; Geiser, Fiona; Lee, James; Cox, Geoffey; Dapremont, Olivier; Suteu, Christina; Assenza, Sebastian P.; Hariharan, Shankar; Nair, Usha
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

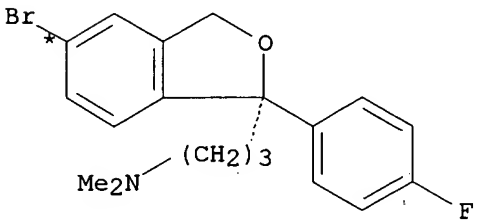
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006449	A1	20030123	WO 2002-DK491	20020712
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2451124	AA	20030123	CA 2002-2451124	20020712
EP 1409472	A1	20040421	EP 2002-750836	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002010817	A	20040622	BR 2002-10817	20020712
CN 1527825	A	20040908	CN 2002-813998	20020712
JP 2004538276	T2	20041224	JP 2003-512221	20020712
ZA 2003009471	A	20041206	ZA 2003-9471	20031205
BG 108572	A	20050331	BG 2004-108572	20040209
US 2005065207	A1	20050324	US 2004-483824	20040930
PRIORITY APPLN. INFO.:			DK 2001-1101	20010713
			DK 2001-1851	20011211
			DK 2001-1852	20011211
			WO 2002-DK491	20020712

GI

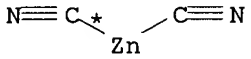
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel method is provided for the manufacture of the antidepressant escitalopram, i.e., (S)-I. The method comprises chromatog. separation of the enantiomers of either (1) citalopram, i.e., (±)-I, or (2) an intermediate in its production, using a chiral stationary phase such as Chiralpak AD or Chiralcel OD. Novel chiral intermediates for the synthesis of escitalopram, made by said method, are also provided. For example, the intermediate nitrile diol (±)-II was resolved using Chiralpak AD stationary phase on a Novasep Licosep 10-50 simulated moving bed chromatograph with MeCN mobile phase at 30°, to give both enantiomers of II with purity exceeding 99% ee. Similarly resolved in 96-99% yield and >99% ee were bromide diol (±)-III and bromophthalane (±)-IV, using Chiralpak AD and Chiralcel OD, resp. Resolution of (±)-IV was performed on a 500-g scale using 98:2 isohexane/isopropanol (vol/vol), and also on a smaller scale using supercrit. CO2 with MeOH/Et2NH/CF3CO2H modifier. The obtained bromide (S)-(+)-IV underwent cyanation by Zn(CN)2 and Pd(PPh3)4 according to the method of WO 00/13648, giving escitalopram in 80% yield and 99.6% ee.

RX(1) OF 1 **A** + B ===> **C**



A



B

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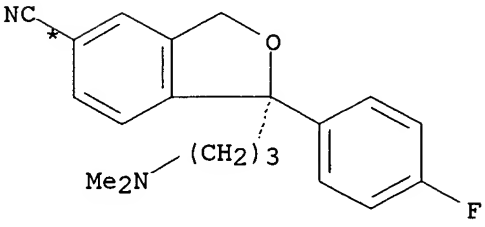


C
YIELD 80%

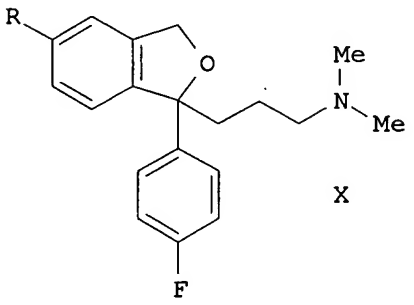
RX(1) RCT A **488148-14-7**, B 557-21-1
PRO C **128196-01-0**
CAT 14221-01-3 Pd(PPh3)4
NTE literature prepn., WO 00/13648, 99.6% ee, no exptl. detail
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searcher : Shears 571-272-2528

L29 ANSWER 9 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:55857 CASREACT
TITLE: Process for the preparation of citalopram
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: Brit. UK Pat. Appl., 11 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2376945	A1	20021231	GB 2001-15708	20010627

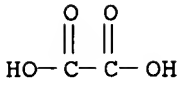
PRIORITY APPLN. INFO.: GB 2001-15708 20010627
OTHER SOURCE(S): MARPAT 138:55857
GI



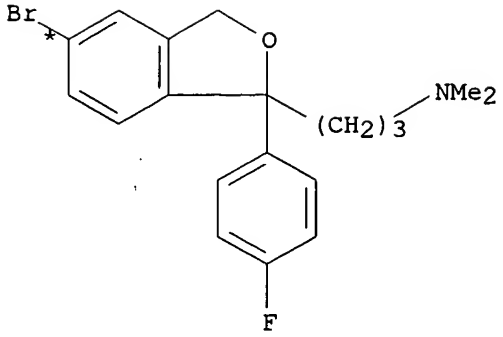
I

AB An improved process for the preparation of citalopram via substitution of the halogen of halophthalane salts I (R = halogen; X = oxalate, fumarate, maleate, citrate, acetate, formate, hydrochloride, hydrobromide, sulfate) using cuprous cyanide in an organic solvent. Thus, bromophthalane oxalate I (R = Br, X = oxalate) was reacted CuCN in diglyme under a nitrogen atmospheric at 150-155° for 3 h to form citalopram which was converted to its HBr salt I (R = CN, X = HBr).

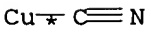
RX(1) OF 2 **A** + B ===> **C**



A: CM 1



A: CM 2



B

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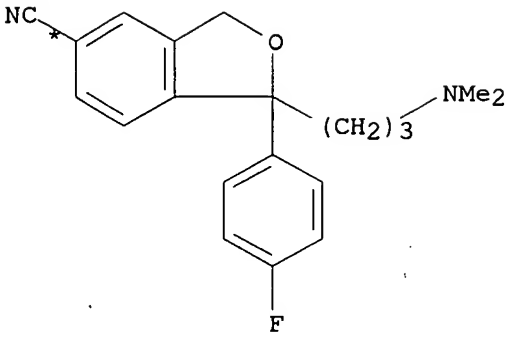


C

RX(1) RCT A **64372-43-6**, B 544-92-3
PRO C **59729-33-8**
SOL 111-96-6 (MeOCH2CH2)2O
CON SUBSTAGE(1) room temperature -> 155 deg C
SUBSTAGE(2) 3 hours, 155 deg C
NTE thermal
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

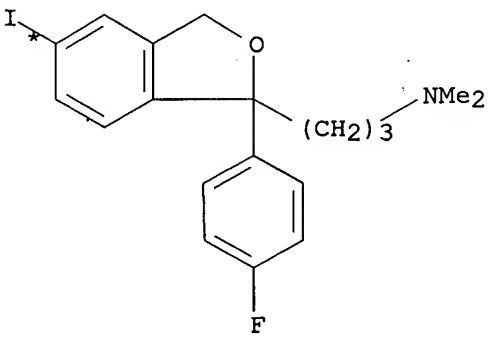
L29 ANSWER 10 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:232543 CASREACT
TITLE: Cyanation process for the preparation of citalopram
INVENTOR(S): Biswas, Sujay; Sharma, Tarun Kant; Kumar, Yatendra; Sathyanarayana, Swargam; Vijayaraghavan, Bakthavathsalan
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

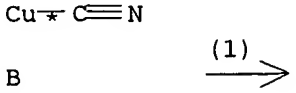
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072565	A1	20020919	WO 2002-IB690	20020308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439856	AA	20020919	CA 2002-2439856	20020308
EP 1370545	A1	20031217	EP 2002-702634	20020308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1496358	A	20040512	CN 2002-806116	20020308
BR 2002007895	A	20041228	BR 2002-7895	20020308
JP 2005500256	T2	20050106	JP 2002-571481	20020308
US 2005085534	A1	20050421	US 2003-469329	20020308
PRIORITY APPLN. INFO.:			IN 2001-DE264	20010309
			WO 2002-IB690	20020308

AB An improved and industrially advantageous process for the preparation of citalopram and pharmaceutically acceptable acid addition salts consists of reacting a precursor substituted with a bromo or an iodo group in the same position as the cyano group in citalopram with a cyanide source in a solvent in the present of a N-containing base; the citalopram free base may then be salified with a pharmaceutically acceptable acids.

RX(1) OF 3 **A** + B ===> **C**...

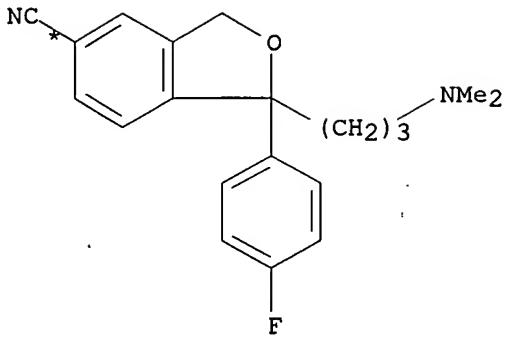


A



B

Searcher : Shears 571-272-2528



C

RX(1) RCT A **260066-78-2**, B 544-92-3
RGT D 110-86-1 Pyridine
PRO C **59729-33-8**
SOL 68-12-2 DMF
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 11 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:216863 CASREACT
TITLE: Preparation of phthalanes
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dhanmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

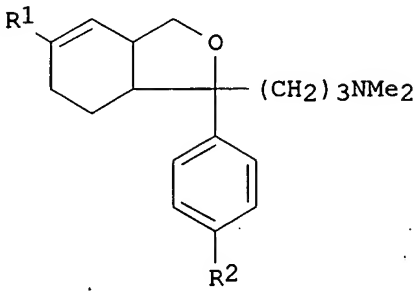
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070501	A1	20020912	WO 2002-GB1054	20020307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442613	AA	20020912	CA 2002-2442613	20020307
EP 1366034	A1	20031203	EP 2002-702553	20020307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

EE 200300424	A	20031215	EE 2003-424	20020307
TR 200301444	T2	20040921	TR 2003-20030144	20020307
LT 5167	B	20041025	LT 2003-86	20030930
BG 108232	A	20050430	BG 2003-108232	20031006
LV 13132	B	20040620	LV 2003-107	20031007
ZA 2003008039	A	20041117	ZA 2003-8039	20031016
US 2004092755	A1	20040513	US 2003-471052	20031118
US 6903228	B2	20050607		

PRIORITY APPLN. INFO.: GB 2001-5627 20010307
WO 2002-GB1054 20020307

OTHER SOURCE(S): MARPAT 137:216863

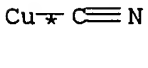
GI



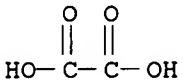
I

AB Citalopram and other phthalanes I [R1 = CN, R2 = halogen, trifluoromethyl, CN, acyl] are made by treating a salt of I [R1 = halogen] with cuprous cyanide. Thus, 100g I.oxalate [R1 = Br, R2 = F] was treated with 35 g CuCN in diglyme at 150-155° for 3 h to give 35 g I [R1 = CN, R2 = F] as the hydrobromide.

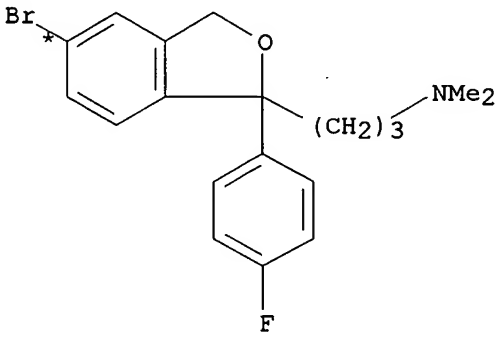
RX(1) OF 1 A + **B** ===> **C**



A



B: CM 1



B: CM 2

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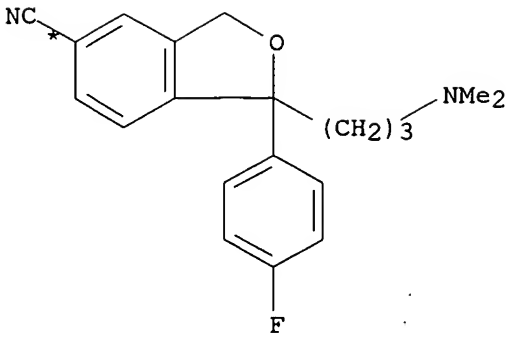
Searcher : Shears 571-272-2528



● HBr

C

RX(1) RCT A 544-92-3, B **64372-43-6**

STAGE(1)
SOL 111-96-6 (MeOCH2CH2)2O

STAGE(2)
RGT D 107-15-3 H2NCH2CH2NH2
SOL 7732-18-5 Water

PRO C **59729-32-7**
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 12 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:78853 CASREACT
TITLE: Preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran.
INVENTOR(S): Petersen, Hans; Ahmadian, Haleh
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: Patentschrift (Switz.), 15 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 691969	A	20011215	CH 2001-1522	20010816
CA 2354877	AA	20020218	CA 2001-2354877	20010809
FI 2001001621	A	20020219	FI 2001-1621	20010809
FI 2001001622	A	20020219	FI 2001-1622	20010809
CA 2354880	C	20030603	CA 2001-2354880	20010809
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IT 2001MI1785	A1	20020218	IT 2001-MI1785	20010813

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NO	2001003942	A	20020219	NO	2001-3942	20010814
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US	6426422	B2	20020730			
US	2002026062	A1	20020228	US	2001-930110	20010814
US	6509483	B2	20030121			
WO	2002016341	A1	20020228	WO	2001-DK541	20010814
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AT	281448	E	20041115	AT	2001-957786	20010814

Searcher : Shears 571-272-2528

PT 1309581	T	20050331	PT 2001-957785	20010814
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ES 2228920	T3	20050416	ES 2001-1957786	20010814
ES 2230347	T3	20050501	ES 2001-1957785	20010814
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NL 1018776	C1	20011024	NL 2001-1018776	20010816
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FR 2813077	A1	20020222	FR 2001-10855	20010816
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FR 2813078	A1	20020222	FR 2001-10857	20010816
FR 2813078	B1	20040402		
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DE 10140029	A1	20020502	DE 2001-10140029	20010816
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CN 1339436	A	20020313	CN 2001-133948	20010817
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ES 2170734	A1	20020801	ES 2001-1919	20010817
ES 2170735	A1	20020801	ES 2001-1920	20010817
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BR 2001005022	A	20020604	BR 2001-5022	20010824
HK 1047086	A1	20050422	HK 2002-106522	20020904
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PRIORITY APPLN. INFO.:			DK 2000-1231	20000818
			WO 2001-DK541	20010814
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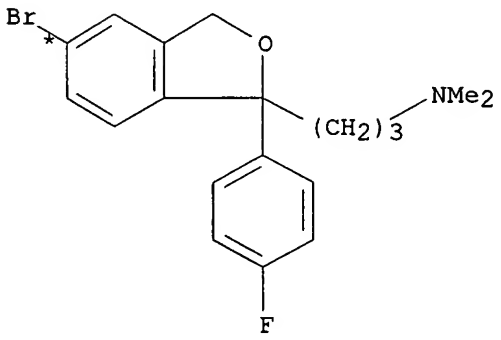
AB Citalopram (I) was prepared by converting a 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran to the 5-carboxylic acid derivative and converting the latter to I. Thus, 5-bromo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran in Me3COMe at -78° was treated with BuLi followed by stirring for 2 h at -30°. Solid CO2 was added followed by stirring for 16 h at room temperature to give 5-carboxy-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran. The latter was heated with sulfamide and SOCl2 in sulfolane at 130° for 2 h to give I.

RX(3) OF 3 COMPOSED OF RX(2), RX(1)
RX(3) **F** + G ===> **B**



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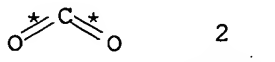
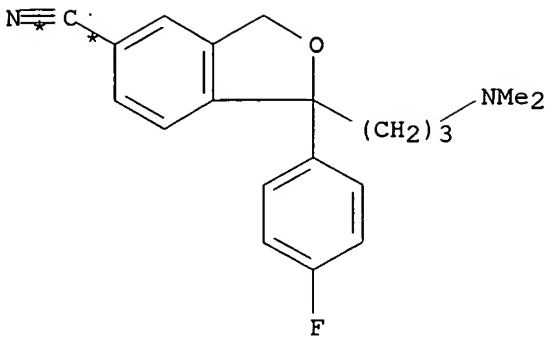


G

2 STEPS



B

RX(2) RCT F **64169-39-7**, G 124-38-9
RGT H 109-72-8 BuLi
PRO A 440121-09-5
SOL 1634-04-4 t-BuOMe
NTE -78° to room temp.

RX(1) RCT A 440121-09-5
RGT C 7803-58-9 (NH2)2SO2, D 7719-09-7 SOCl2
PRO B **59729-33-8**
SOL 126-33-0 Sulfolane
NTE 130°

L29 ANSWER 13 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:137393 CASREACT
Correction of: 134:353251
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans; Rock, Michael Harold
PATENT ASSIGNEE(S): H Lundbeck A/S, Den.
SOURCE: Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2354240	A1	20010321	GB 2001-1508	19991119
GB 2354240	B2	20010523		
IT 99MI1579	A1	20010115	IT 1999-MI1579	19990715
WO 2000011926	A2	20000309	WO 1999-DK643	19991119
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,

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AT 213237		E	20020215	AT 1999-968206	19991119
BR 9917367		A	20020305	BR 1999-17367	19991119
AT 9909040		A	20020515	AT 1999-9040	19991119
AT 409960		B	20021227		
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JP 2002523432		T2	20020730	JP 2000-567065	19991119
JP 3389571		B2	20030324		
PT 1105382		T	20020731	PT 1999-968206	19991119
ES 2172356		T3	20020916	ES 1999-968206	19991119
CZ 292174		B6	20030813	CZ 2001-319	19991119
CN 1129593		B	20031203	CN 1999-816768	19991119
NZ 514982		A	20040130	NZ 1999-514982	19991119
CA 2290125		C	20040810	CA 1999-2290125	19991122
CA 2290125		AA	20001225		
NO 2001000318		A	20010220	NO 2001-318	20010119
SE 2001000194		A	20010425	SE 2001-194	20010124
SE 516689		C2	20020212		
FI 2001000154		A	20010209	FI 2001-154	20010125
FI 108538		B1	20020215		
ZA 2001007956		A	20020927	ZA 2001-7956	20010927
ZA 2001008855		A	20020611	ZA 2001-8855	20011026
US 2002061925		A1	20020523	US 2001-12025	20011106
US 6750358		B2	20040615		
BG 106190		A	20020830	BG 2001-106190	20011207
ZA 2002005023		A	20030623	ZA 2002-5023	20020621
HK 1047745		A1	20040910	HK 2002-109330	20021224
PRIORITY APPLN. INFO.:				DK 1999-921	19990625
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OTHER SOURCE(S): MARPAT 135:137393

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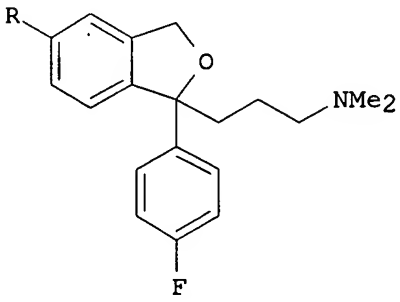
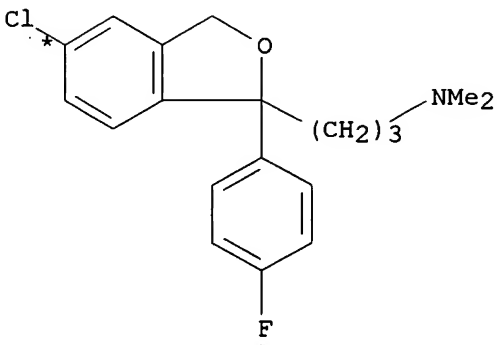


I

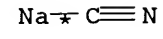
AB A method for preparing the antidepressant, citalopram [I; R = CN], by reacting an isobenzofuranpropanamine [I; R = Cl or Br] with a cyanide source in the presence of a nickel catalyst is presented. Citalopram is produced in high yield as a very pure product using this catalytic process. Thus, sequential addition of I (R = Cl) and NaCN to the Ni catalyst formed by reflux of NiCl2 with PPh3 in AcCN in the presence

of a catalytic amount of Zn, followed by workup and treatment with oxalic acid, gave citalopram oxalate in 55% yield.

RX(1) OF 1 **A** + B ===> **C**



A



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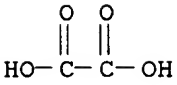

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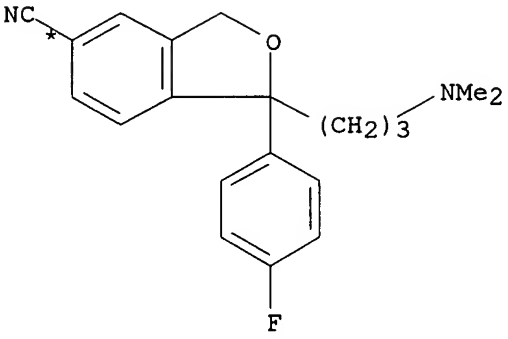
YIELD 55%



C: CM 2
YIELD 55%

RX(1) RCT A **64169-45-5**

STAGE(1)
RGT D 603-35-0 PPh3
CAT 7718-54-9 NiCl2
SOL 75-05-8 MeCN

STAGE(2)
CAT 7440-66-6 Zn

Searcher : Shears 571-272-2528

STAGE(3)
RCT B 143-33-9

PRO C **207559-01-1**
NTE 1st step is catalyst prepn.; reflux

L29 ANSWER 14 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:61225 CASREACT
TITLE: Process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation
INVENTOR(S): Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico
PATENT ASSIGNEE(S): H. Lundbeck A/s, Den.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047877	A2	20010705	WO 2001-DK148	20010307
WO 2001047877	A3	20001227		
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SK 284418	B6	20050401	SK 2001-1847	20010307
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CH 691999	A	20010726	CH 2001-1412	20010726
ES 2170733	A1	20020801	ES 2001-1763	20010727
ES 2170733	B1	20031216		
AU 750006	B1	20020711	AU 2001-65478	20010827
SE 2001003044	A	20020629	SE 2001-3044	20010914
ZA 2001010133	A	20030113	ZA 2001-10133	20011210
BG 106219	A	20020830	BG 2001-106219	20011213
US 2002087012	A1	20020704	US 2001-35005	20011220
US 6855834	B2	20050215		
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US 2003178295	A1	20030925	US 2003-361800	20030210
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OTHER SOURCE(S): MARPAT 135:61225

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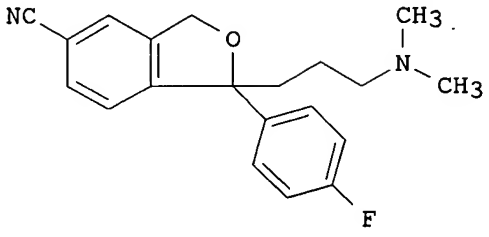

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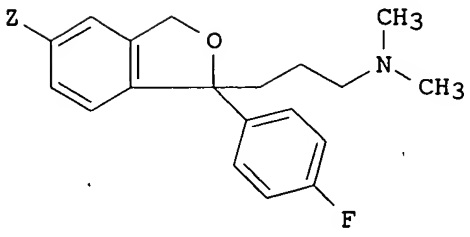
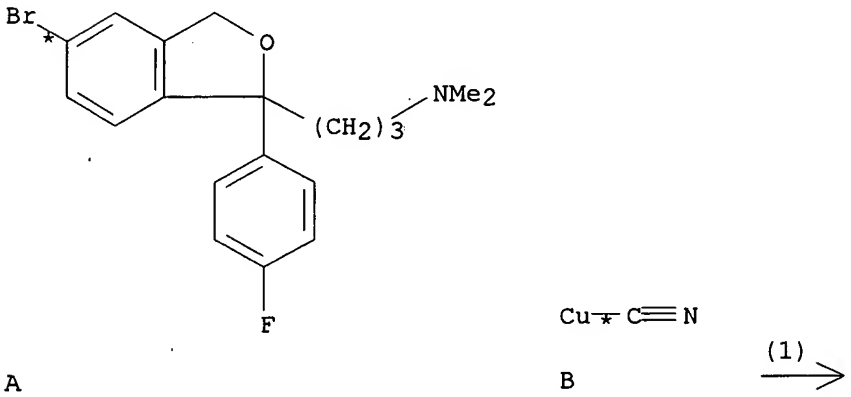


II

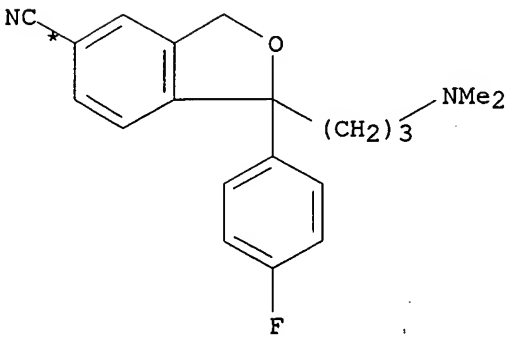
Searcher : Shears 571-272-2528

AB High-purity citalopram (I) is prepared on an industrial scale by: subjecting a citalopram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalopram product is optionally subjected to some initial purification and the crude citalopram base is subsequently subjected to a thin- or falling-film distillation process.

RX(1) OF 1 **A** + B ===> **C**



A B



C

RX(1) RCT A **64169-39-7**, B 544-92-3
PRO C **59729-33-8**
SOL 126-33-0 Sulfolane
NTE thin-film distn. purifn.

L29 ANSWER 15 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:61224 CASREACT
TITLE: Method for the preparation and purification of citalopram

INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045483	A2	20010628	WO 2001-DK147	20010307
WO 2001045483	A3	20011227		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2360303	AA	20010628	CA 2001-2360303	20010307
CA 2360303	C	20030812		
EP 1181713	A2	20020227	EP 2001-913726	20010307
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BR 2001006272	A	20040615	BR 2001-6272	20010307
EP 1462447	A2	20040929	EP 2004-4482	20010307
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ES 2170732	A1	20020801	ES 2001-1762	20010727

AU 744112	B1	20020214	AU 2001-65477	20010827
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HR 2002000004	A1	20030430	HR 2002-4	20020104
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US 6455710	B2	20020924		

PRIORITY APPLN. INFO.:

DK 2000-1929	20001222
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OTHER SOURCE(S): MARPAT 135:61224

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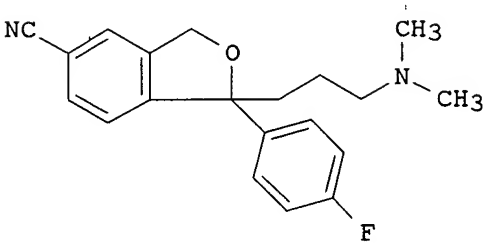

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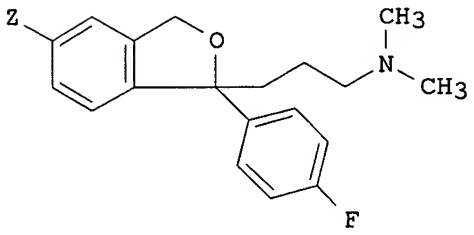
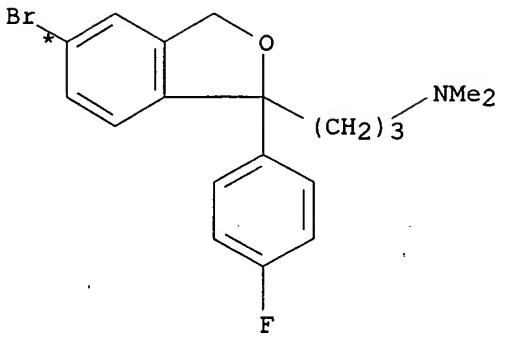


II

AB A process for the preparation and purification of citalopram (I) is presented in which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization and recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

RX(1) OF 1 **A** + B ===> **C**



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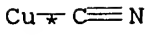

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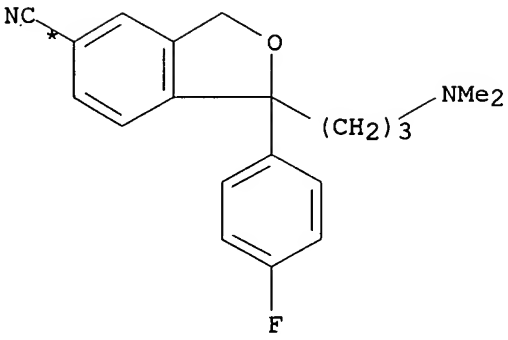

C

RX(1) RCT A **64169-39-7**, B 544-92-3
PRO C **59729-33-8**
SOL 126-33-0 Sulfolane

L29 ANSWER 16 OF 16 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:194283 CASREACT
TITLE: Method for the preparation of citalopram
INVENTOR(S): Petersen, Hans; Rock, Michael Harold; Svane, Henrik
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000013648	A2	20000316	WO 1999-DK640	19991122
WO 2000013648	A3	20000713		

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IT	99MI1581	A1	20010115	IT 1999-MI1581	19990715
ES	2169709	A1	20020701	ES 2001-50056	19991025
JP	2003012663	A2	20030115	JP 2002-106016	19991025
EP	1298124	A1	20030402	EP 2002-28326	19991025

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CN	1550497	A	20041201	CN 2003-200316503319991025	
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CN	1502616	A	20040609	CN 2003-10118780	19991122
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HK	1049002	A1	20041231	HK 2003-101234	20030218

PRIORITY APPLN. INFO.:

DK	1999-920	19990625
EP	1999-950511	19991025
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CN	1999-816751	19991122
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WO	1999-DK640	19991122

OTHER SOURCE(S): MARPAT 132:194283

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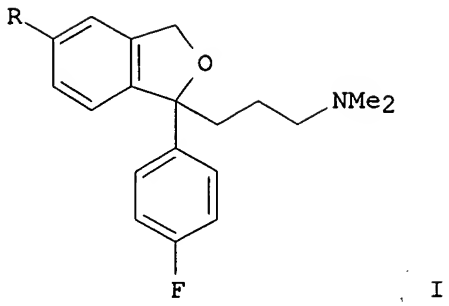
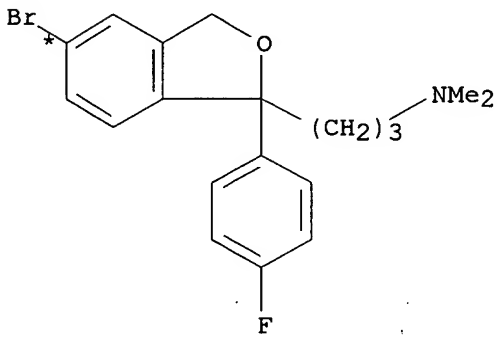


I

AB The title compound [I; R = CN], the well known antidepressant (no data), was prepared by reacting a compound I [wherein R = halo, CF3(CF2)nSO2; n = 0-8] with a cyanide source in the presence of a palladium catalyst and a catalytic amount of Cu+ or Zn2+, or with Zn(CN)2 in the presence of a palladium catalyst.

RX(1) OF 2 **A** + B ===> **C**



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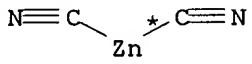

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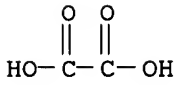

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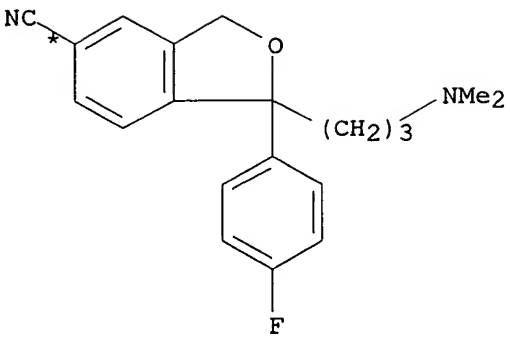
YIELD 92%



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RX(1) RCT A **64169-39-7**, B 557-21-1
PRO C **207559-01-1**
CAT 14221-01-3 Pd(PPh3)4
SOL 68-12-2 DMF

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COPYRIGHT (C) 2005 THE THOMSON CORPORATION

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COPYRIGHT (C) FIZ-CHEMIE BERLIN

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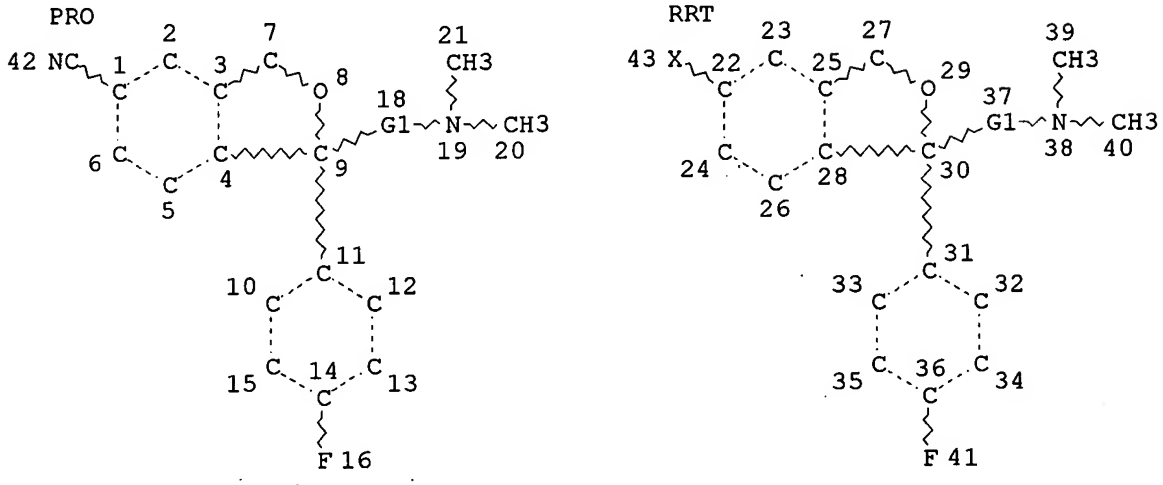

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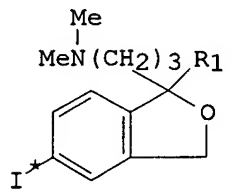
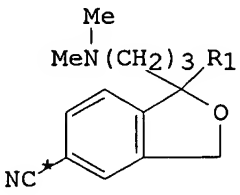
NUMBER OF NODES IS 42

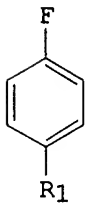
STEREO ATTRIBUTES: NONE
L31 1 SEA L28

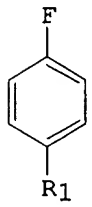
L31 ANSWER 1 OF 1 DJSMDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004:1382 DJSMDS
TI AR . NITRILES FROM HALIDES
PA Ranbaxy, Lab, Ltd (Biswas, S., et al.)
PI WO 200272565
DT Patent
VI 30-5
OS WPI 2002-691800
AB cf. 1999:2447; 2002:1070; 2001:0701. Expensive palladium catalysts are not required in this method. For further examples, see citation 1.

RX(1) OF 1 **A** ===> **B**









A (1) → B
YIELD 94.0%

RX(1) RCT A, **129111**; 7.5 g
SOL 23, DMF
CAT 172, Cuprous; 2.4 g
10, Pyridine; 5.6 g
PRO B, **102487**; HBr salt, 6.7 g
T 140.0 - 145.0 Cel
TIM 3.0 hr
CMT Rinsed with aq. NH4OH and H2O, solvent removed, diluted with toluene, 3.6 g HBr added
CMT Path A

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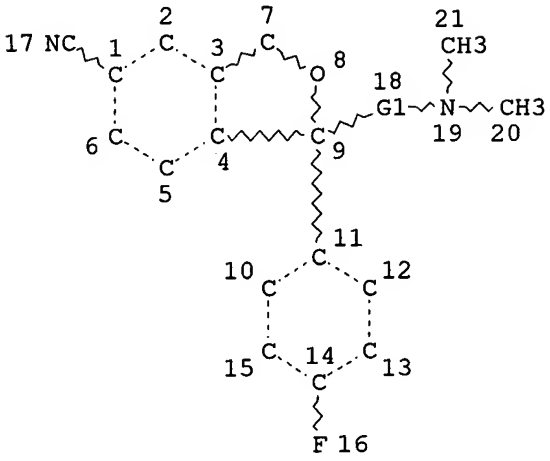

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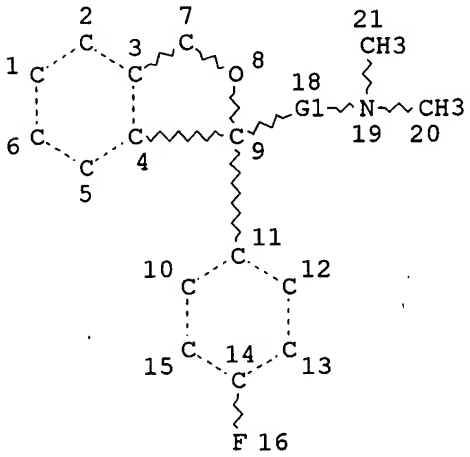

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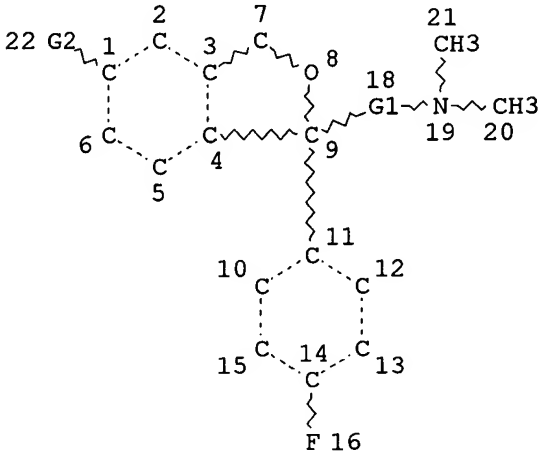

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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE

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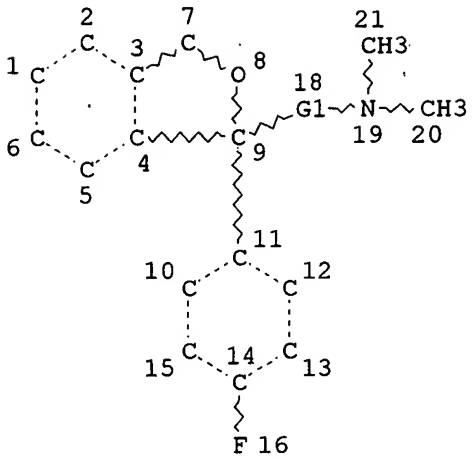

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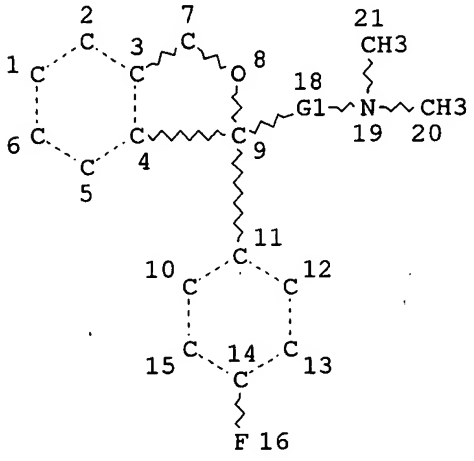

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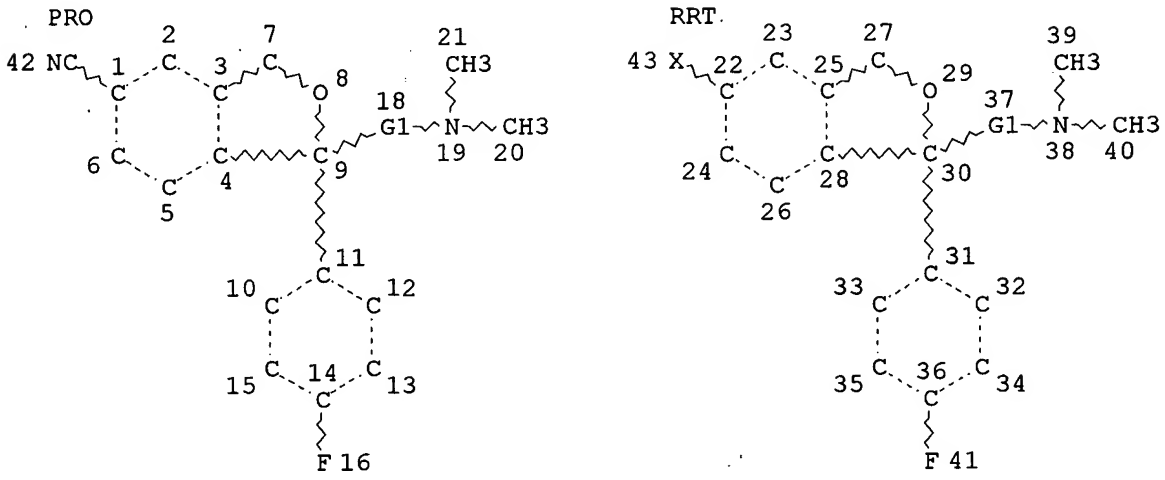

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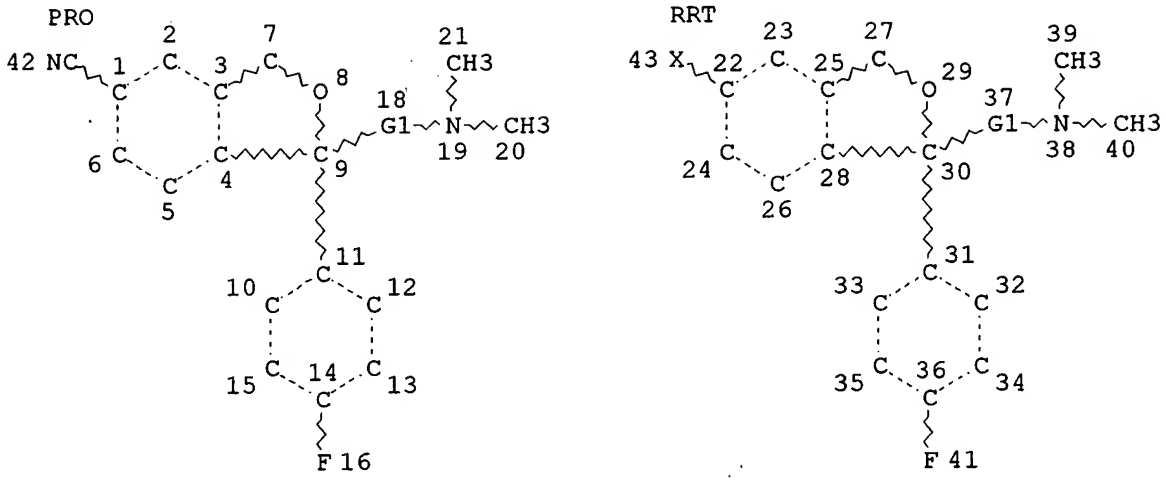

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L*** DEL 10 S L7 NOT PY=>2002
L*** DEL 10 S L7 NOT PD=>20020107
L*** DEL 10 S L8 OR L9

Searcher : Shears 571-272-2528

```
                D 1-10 IBIB ABS

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:50:35 ON 18 OCT 2005
L*** DEL   9905 S L2

     FILE 'REGISTRY' ENTERED AT 12:51:14 ON 18 OCT 2005
L5             6 SEA ABB=ON  PLU=ON  (59729-33-8/BI OR 129356-76-9/BI OR
                 134915-04-1/BI OR 475107-77-8/BI OR 59729-32-7/BI OR
                 64169-59-1/BI)
                 D QUE

     FILE 'CAOLD' ENTERED AT 12:51:43 ON 18 OCT 2005
L6             0 SEA ABB=ON  PLU=ON  L5

     FILE 'USPATFULL' ENTERED AT 12:51:50 ON 18 OCT 2005
L7            73 SEA ABB=ON  PLU=ON  L5/P
L8            10 SEA ABB=ON  PLU=ON  L7 NOT (PY=>2002 OR PD=>20020107)
                 D 1-10 IBIB ABS

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:52:46 ON 18 OCT 2005
L9             0 SEA ABB=ON  PLU=ON  L5(L)(PREP? OR MANUF?)
L10          387 SEA ABB=ON  PLU=ON  L5 AND (PREP? OR MANUF?)
                 D KWIC
                 D KWIC 2

     FILE 'MARPAT' ENTERED AT 12:54:41 ON 18 OCT 2005
                 D L1
L11            0 SEA SSS SAM L1 (MODIFIED ATTRIBUTES)
L12            7 SEA SSS FUL L1 (MODIFIED ATTRIBUTES)

     FILE 'MARPAT' ENTERED AT 12:55:24 ON 18 OCT 2005
                 D QUE STAT
                 D 1-7 .BEVMAR1

     FILE 'MARPATPREV' ENTERED AT 12:55:27 ON 18 OCT 2005
                 D QUE L1

     FILE 'MARPAT' ENTERED AT 12:57:33 ON 18 OCT 2005
L13              STR L1
L14            1 SEA SSS SAM L13 (MODIFIED ATTRIBUTES)
L15           25 SEA SSS FUL L13 (MODIFIED ATTRIBUTES)
L16              STR L13
L17           16 SEA SUB=L15 SSS FUL L16 (MODIFIED ATTRIBUTES)
                 D QUE STAT
                 D 1-16 .BEVMAR1

     FILE 'MARPATPREV' ENTERED AT 12:59:28 ON 18 OCT 2005
L18            0 SEA SSS FUL L13 (MODIFIED ATTRIBUTES)
                 D QUE STAT

     FILE 'CASREACT' ENTERED AT 13:01:04 ON 18 OCT 2005
L19              STR L13
L20            4 SEA SSS SAM L19 (    25 REACTIONS)
L21           46 SEA SSS FUL L19 (   208 REACTIONS)
L22              STR L19
L23            0 SEA SSS SAM L22 (     0 REACTIONS)
L24            0 SEA SUB=L21 SSS FUL L22 (     0 REACTIONS)
L25              STR L22
L26           45 SEA SUB=L21 SSS FUL L25 (   149 REACTIONS)
```

```
                D FHIT
                D FHIT 2
L27             STR L22
L28             STR L22
L29          16 SEA SUB=L21 SSS FUL L28 (    19 REACTIONS)
                D QUE STAT
                D 1-16 IBIB ABS FHIT

     FILE 'DJSMDS, CHEMINFORMRX' ENTERED AT 13:05:16 ON 18 OCT 2005
L30           1 SEA ABB=ON  PLU=ON  L28
L31           1 SEA ABB=ON  PLU=ON  L28
                D QUE STAT
                D BIB AB FHIT

     FILE 'HOME' ENTERED AT 13:06:44 ON 18 OCT 2005
                D QUE STAT L2
                D QUE STAT L17
                D QUE STAT L18
                D QUE STAT L29
                D QUE STAT L31


     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   17 OCT 2005  HIGHEST RN 865410-76-0
     DICTIONARY FILE UPDATES:  17 OCT 2005  HIGHEST RN 865410-76-0

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************

     Structure search iteration limits have been increased.  See HELP SLIMI
     for details.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE CAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
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FILE COVERS 1907 - 18 Oct 2005 VOL 143 ISS 17
FILE LAST UPDATED: 17 Oct 2005 (20051017/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply They are available for your review at:

http://www.cas.org/infopolicy.html

FILE CAOLD
FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US6957446
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229280
CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

>>> USPAT2 is now available. USPATFULL contains full text of the
>>> original, i.e., the earliest published granted patents or
>>> applications. USPAT2 contains full text of the latest US
>>> publications, starting in 2001, for the inventions covered in
>>> USPATFULL. A USPATFULL record contains not only the original
>>> published document but also a list of any subsequent
>>> publications. The publication number, patent kind code, and
>>> publication date for all the US publications for an invention
>>> are displayed in the PI (Patent Information) field of USPATFULL
>>> records and may be searched in standard search fields, e.g., /PN,
>>> /PK, etc.

>>> USPATFULL and USPAT2 can be accessed and searched together
>>> through the new cluster USPATALL. Type FILE USPATALL to
>>> enter this cluster.
>>>

Searcher : Shears 571-272-2528

>>> Use USPATALL when searching terms such as patent assignees,
>>> classifications, or claims, that may potentially change from
>>> the earliest to the latest publication.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE MEDLINE
FILE LAST UPDATED: 15 OCT 2005 (20051015/UP). FILE COVERS 1950 TO DA

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 13 Oct 2005 (20051013/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE MARPAT
FILE CONTENT: 1988-PRESENT (VOL 143 ISS 15)(20051016/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6916824 12 JUL 2005
DE 1020040544 28 JUL 2005
EP 1555012 20 JUL 2005
JP 2005191426 14 JUL 2005
WO 2005079855 01 SEP 2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Searcher : Shears 571-272-2528

FILE MARPATPREV
FILE COVERS CURRENT RECORDS AND IS UPDATED DAILY
FILE LAST UPDATED: 18 OCT 2005(20051018)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6797117 28 SEP 2004
DE 10322109 4 MAY 2004
EP 1491180 29 DEC 2004
JP 2004196848 15 JUL 2004
WO 2005079855 1 SEP 2005

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FILE CASREACT
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FILE CONTENT:1840 - 16 Oct 2005 VOL 143 ISS 16

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 9.2 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1 provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substanc identification.

FILE DJSMDS
FILE LAST UPDATED: 30 AUG 2005 <20050830/UP>

>>> DERWENT JOURNAL OF SYNTHETIC METHODS - DERWENT SUBSCRIBER FILE >>>
>>> FILE COVERS 1975 TO 2004 DATA <<<
>>> GRAPHIC IMAGES OF THE PRINTED DERWENT JOURNAL OF SYNTHETIC METHODS ARE AVAILABLE FROM 1975 TO 2004 <<<
>>> PLEASE NOTE: IN DJSM HYDROGEN BONDS CANNOT BE DEFINED AS REACTION SITES <<<

FILE CHEMINFORMRX
FILE LAST UPDATED: 15 SEP 2005 <20050915/UP>

>>> CAS Registry Numbers are available for substances prior to 1995 <<<

FILE HOME